=> b medline caplus lifesci embase uspatfull biosis

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 10:44:47 ON 24 MAY 2002

FILE 'CAPLUS' ENTERED AT 10:44:47 ON 24 MAY 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'LIFESCI' ENTERED AT 10:44:47 ON 24 MAY 2002
COPYRIGHT (C) 2002 Cambridge Scientific Abstracts (CSA)

FILE 'EMBASE' ENTERED AT 10:44:47 ON 24 MAY 2002
COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved.

FILE 'USPATFULL' ENTERED AT 10:44:47 ON 24 MAY 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 10:44:47 ON 24 MAY 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

=> s (insulin()like()growth()factor()binding()protein()5) or (IGF()bindging()protein()5) or IGFBP5 or (IGFBP)5) or IBP5 or (ibp()5)

5 FILES SEARCHED...
L1 2494 (INSULIN(W) LIKE(W) GROWTH(W) FACTOR(W) BINDING(W) PROTEIN(W) 5) OR (IGF(W) BINDGING(W) PROTEIN(W) 5) OR IGFBP5 OR (IGFBP(W) 5) OR IBP5 OR (IBP(W) 5)

=> s l1 and (antisens? or ribozym? or triplex)

L2 84 L1 AND (ANTISENS? OR RIBOZYM? OR TRIPLEX)

=> dup rem l2

PROCESSING COMPLETED FOR L2
L3 42 DUP REM L2 (42 DUPLICATES REMOVED)

=> d l3 ibib abs tot

L3 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:314486 CAPLUS
DOCUMENT NUMBER: 136:321297
TITLE: Use of pregnancy-associated plasma protein A (PAPP-A2), a novel **insulin like growth factor-binding protein-5** proteinase, for diagnosis and treatment of fetal abnormalities
INVENTOR(S): Oxvig, Claus; Overgaard, Michael Toft
PATENT ASSIGNEE(S): Combi Biotech Aps, Den.
SOURCE: PCT Int. Appl., 113 pp.

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032953	A2	20020425	WO 2001-DK685	20011019

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DK 2000-1571 A 20001020
US 2000-241840P P 20001020

AB The present invention provides nucleotide and amino acid sequences that identify and encode a new protein with homol. to pregnancy-assocd. plasma protein-A (PAPP-A). We denote this protein PAPP-A2. The cDNA encoding PAPP-A2 was derived from human placenta. The present invention also provides for **antisense** mols. to the nucleotide sequences which encode PAPP-A2 and expression vectors for the prodn. of purified PAPP-A2. Antibodies, capable of binding specifically to PAPP-A2, and hybridization probes or oligonucleotides for the detection of PAPP-A2-encoding nucleotide sequences are also provided. Genetically engineered host cells for the expression of PAPP-A2 and use of the protein to produce antibodies capable of binding specifically to the protein are another embodiment of the present invention. Methods of screening for pathologies in pregnant and non-pregnant patients that are based on detection of PAPP-A2 antigen in human body fluids or PAPP-A2-encoding nucleic acid mols are provided. Use of the protein to screen for agents that alter the protease activity of PAPP-A2, use of the protein as a therapeutic target for such agents, and use of the protein as a therapeutic agent in relevant pathol. states are other objects of the invention. Methods for screening for altered focal proliferation states in pregnant and/or non-pregnant patients, which include detecting levels of PAPP-A2, are also described. The present invention also provides the identification of a natural substrate of PAPP-A2, insulin-like growth factor binding protein (**IGFBP**)-**5**.

L3 ANSWER 2 OF 42 USPATFULL
ACCESSION NUMBER: 2002:99890 USPATFULL
TITLE: HER -2/neu overexpression abrogates growth inhibitory pathways
INVENTOR(S): Slamon, Dennis J., Woodland Hills, CA, UNITED STATES
Wilson, Cindy A., Los Angeles, CA, UNITED STATES
Calzone, Frank J., Westlake Village, CA, UNITED STATES
PATENT ASSIGNEE(S): The Regents of the University of California and Amgen Inc. (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 20020051785	A1	20020502	
APPLICATION INFO.:	US 2001-813517	A1	20010320	(9)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2000-190598P	20000322	(60)

DRIVE WEST, SUITE 1050, LOS ANGELES, CA, 90045
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 2765
AB The present invention provides methods for obtaining genetic profiles of
cancer cells in order to assess the status of a cancer in an individual.
In addition, the present invention provides methods for inhibiting the growth of cancer cells that exhibit certain genetic profiles. These methods identify an important link between HER-2/neu overexpression and loss of growth inhibition by the TGF-.beta. signaling pathway in cancer cells. Compositions as well as therapeutic and diagnostic methodologies based on this disclosure are provided.

L3 ANSWER 3 OF 42 USPATFULL
ACCESSION NUMBER: 2002:16859 USPATFULL
TITLE: Metastatic breast and colon cancer regulated genes
INVENTOR(S): Riese, Klaus, Berlin, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20020009739	A1	20020124
APPLICATION INFO.:	US 2001-827669	A1	20010406 (9)
RELATED APPLN. INFO.:	Division of Ser. No. US 1999-417615, filed on 13 Oct 1999, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-164351P	19991015 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Chiron Corporation, Intellectual Property R338, P.O. Box 8097, Emeryville, CA, 94662-8097
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 3011
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Gene sequences as shown in SEQ ID NOS: 1-85 have been found to be significantly associated with metastatic potential of cancer cells, especially breast and colon cancer cells. Methods are provided for determining the risk of metastasis of a tumor, which involve determining
whether a tissue sample from a tumor expresses a polypeptide encoded by a gene as shown in SEQ ID NOS: 1-85, or a substantial portion thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 42 USPATFULL
ACCESSION NUMBER: 2002:[illegible] USPATFULL
TITLE: Polynucleotides, polypeptides expressed by the polynucleotides and methods for their use
INVENTOR(S): Watson, John D., Auckland, NEW ZEALAND
Morrison, James G., Auckland, NEW ZEALAND
PATENT ASSIGNEE(S): Genesis Research & Development Corporation Ltd., NEW ZEALAND (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6[illegible]360	B1	20020430
APPLICATION INFO.:	US 2[illegible]-724864		20001128 (9)

PRIORITY INFORMATION: US 1999-171678P 19991222 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Carlson, Karen Cochrane
ASSISTANT EXAMINER: Mitra, Rita
LEGAL REPRESENTATIVE: Speckman, Ann W., Sleath, Janet
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 2
NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)
LINE COUNT: 3737
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel polynucleotides including partial and extended sequences, and open reading frames, are provided, together with probes and primers, DNA constructs comprising the polynucleotides, biological materials and organisms incorporating the polynucleotides, polypeptides expressed by the polynucleotides, and methods for using the polynucleotides and polypeptides.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 5 OF 42 USPATFULL
ACCESSION NUMBER: 2001:75189 USPATFULL
TITLE: Methods and compositions for identifying morphogenic protein analogs using morphogenic protein responsive inhibitory elements
INVENTOR(S): Yeh, Lee-Chuan C., San Antonio, TX, United States
Lee, John C., San Antonio, TX, United States
PATENT ASSIGNEE(S): Stryker Corporation, Kalamazoo, MI, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6309787	B1	20020409
APPLICATION INFO.:	US 1999-465353		19991216 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Riley, Jezia
LEGAL REPRESENTATIVE: Fish & Neave, Haley, Jr., James F., Mangasarian, Karen
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 12 Drawing Figure(s); 13 Drawing Page(s)
LINE COUNT: 1687
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates generally to methods and compositions for identifying morphogenic protein analogs. In one embodiment, this invention relates to an osteogenic protein reponsive transcription inhibitory element. This invention also relates to the identified morphogenic protein analogs which can mimic the biological effects of morphogenic proteins, particularly those relating to the BMP family such as osteogenic protein (OP-1), on the regulation of gene expression and tissue inductive capabilities.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:63856 CAPLUS
DOCUMENT NUMBER: 134:125934
TITLE: **IGFBP-5 antisense** oligodeoxynucleotide therapy for hormone-regulated tumors

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001005435	A2	20010125	WO 2000-CA853	20000719
WO 2001005435	A3	20010322		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1200579	A2	20020502	EP 2000-947725	20000719
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			

PRIORITY APPLN. INFO.: US 1999-144495P P 19990719
WO 2000-CA853 W 20000719

AB A method is provided for treating hormone-regulated tumors (e.g. breast and prostatic tumors) in mammals, including humans, by administration of an **antisense** oligodeoxynuclectide (ODN) which is complementary to a portion of the gene encoding **IGFBP 5**. Using the Shionogi tumor model in vitro and in vivo, the administration of such an ODN was shown to reduce proliferation of tumor cells, and also to delay the progression to androgen independence. Thus, treatment of prostate cancer in mammals, including humans, and delay of the progression of prostate tumors to androgen independence is accomplished by administering to the mammal a therapeutically effective amt. of an **antisense** oligodeoxynucleotide which is complementary to a portion of the nucleic acid sequence encoding **IGFBP-5** and which hybridizes with such a sequence to inhibit expression of **IGFBP-5**. Specific **antisense** ODNs which are suitable for use in the method are GACCACGCTGATCACCAT, which is derived from the murine gene sequence, and CGCGGTGAGCAACACCAT and AGGTCATGCAGCAGCCGC, which are derived from the human gene sequence.

L3 ANSWER 7 OF 42 USPATFULL
ACCESSION NUMBER: 2001:231143 USPATFULL
TITLE: Arrays for identifying agents which mimic or inhibit the activity of interferons
INVENTOR(S): Silverman, Robert H., Beachwood, OH, United States
Williams, Bryan R. G., Cleveland, OH, United States
Der, Sandy, Cleveland, OH, United States
PATENT ASSIGNEE(S): The Cleveland Clinic Foundation, Cleveland, OH, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6331398	B1	20011218
APPLICATION INFO.:	US 1999-414488		19991023 19

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-101437P	19980923 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED

NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 963
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods and model systems for identifying and characterizing new therapeutic agents, particularly proteins, which mimic or inhibit the activity of all interferons, Type I interferons, IFN-.alpha., IFN-.beta., or IFN-.gamma.. The method comprises administering an interferon selected from the group consisting of IFN-.alpha., IFN .beta., IFN-.tau., IFN .omega., IFN-.gamma., and combinations thereof to cultured cells, administering the candidate agent to a duplicate culture of cells; and measuring the effect of the candidate agent and the interferon on the transcription or translation of one or, preferably, a plurality of the interferon stimulated genes or the interferon repressed genes (hereinafter referred to as "ISG's" and "IRGs", respectively). The model system is an array with gene probes that hybridize with from about 100 to about 5000 ISG and IRG transcripts.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 8 OF 42 USPATFULL
ACCESSION NUMBER: 2001:214830 USPATFULL
TITLE: TNF receptor death domain ligand proteins and inhibitors of ligand binding
INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schievella, Andrea R., Winchester, MA, United States
Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6322972	B1	20011127
APPLICATION INFO.:	US 1998-185258		19981102 (9)

RELATED APPLN. INFO.: Division of Ser. No. US 1997-839032, filed on 23 Apr 1997, now patented, Pat. No. US 5891675 Division of Ser. No. US 1996-698551, filed on 15 Aug 1996, now patented, Pat. No. US 5712381, issued on 27 Jan 1998 Continuation-in-part of Ser. No. US 1996-602223, filed on 15 Feb 1996, now patented, Pat. No. US 5843675 Continuation-in-part of Ser. No. US 1995-533901, filed on 26 Sep 1995, now patented, Pat. No. US 5852173 Continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995, now patented, Pat. No. US 5849501 Continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Kim, John
LEGAL REPRESENTATIVE: Lahive & Cockfield, LLP, Mandragouras, Esq., Amy E.
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1639
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are [illegible] and methods of making

TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 9 OF 42 USPATFULL

ACCESSION NUMBER:	2001:71356 USPATFULL		
TITLE:	Methods for the production of biologically active agents contained in an extracellular matrix		
INVENTOR(S):	Keeping, Hugh S., 10 King Philip Ave., Bristol, RI, United States 02809		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6232122	B1	20010515
APPLICATION INFO.:	US 2000-560109		20000530 (9)
	NUMBER		DATE
PRIORITY INFORMATION:	US 1999-137368P		19990603 (60)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Ketter, James		
LEGAL REPRESENTATIVE:	Hifer, Mark A.Brown Rudnick Freed & Gesmer		
NUMBER OF CLAIMS:	25		
EXEMPLARY CLAIM:	1		
LINE COUNT:	715		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to methods for the production in vitro of cell growth supportive surfaces comprising naturally secreted human extracellular matrix material comprising biologically active agents such as growth factors ideally produced and elaborated by the extracellular matrix-secreting cells. The present invention provides an efficient method for improving growth factor potency and extending half-life in order to promote cell attachment, growth and/or differentiation. The surfaces of the present invention enable propagation of difficult cells in culture.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 10 OF 42 USPATFULL

ACCESSION NUMBER:	2001:44138 USPATFULL		
TITLE:	Treatment of partial growth hormone insensitivity syndrome		
INVENTOR(S):	Attie, Kenneth M., San Francisco, CA, United States Carlsson, Lena M. S., Gothenburg, Sweden Gesundheit, Neil, Los Altos, CA, United States Goddard, Audrey, San Francisco, CA, United States		
PATENT ASSIGNEE(S):	Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6207640	B1	20010327
APPLICATION INFO.:	US 1996-643212		19960503 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-410452, filed on 24 Mar 1995, now abandoned Continuation of Ser. No. US 1994-224982, filed on [illegible] Apr 1994, now patented, Pat. [illegible]

PRIMARY EXAMINER: Jones, Dwayne C.
ASSISTANT EXAMINER: Del[redacted]oix-Muirheid, C.
LEGAL REPRESENTATIVE: Kn[redacted], Martens, Olson & Bear, LLP
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 44 Drawing Figure(s); 38 Drawing Page(s)
LINE COUNT: 2465
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for increasing the growth rate of a human patient having partial growth hormone insensitivity syndrome, but not Laron syndrome, are described. One such method comprises administering an effective dose of growth hormone, preferably growth hormone with a native human sequence, with or without an N terminal methionine, to the patient. The patient is characterized as having a height of less than about -3 standard deviations below normal for age and sex, a serum level of high-affinity growth hormone binding protein that is at least 2 standard deviations below normal levels, a serum level of IGF-I that is below normal mean levels, and a serum level of growth hormone that is at least normal. In another such method, the same patient population is treated with an effective amount of IGF-I, given alone or in combination with an amount of growth hormone that is effective in combination with the IGF-I.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 11 OF 42 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001388916 MEDLINE
DOCUMENT NUMBER: 21336417 PubMed ID: 11112656
TITLE: Novel therapeutic strategy for advanced prostate cancer using **antisense** oligodeoxynucleotides targeting anti-apoptotic genes upregulated after androgen withdrawal to delay androgen-independent progression and enhance chemosensitivity.
AUTHOR: Miyake H; Hara I; Kamidono S; Gleave M E
CORPORATE SOURCE: The Prostate Center, Vancouver General Hospital, Vancouver, Canada.. hideakimiyake@hotmail.com
SOURCE: INTERNATIONAL JOURNAL OF UROLOGY, (2001 Jul) 8 (7) 337-49. Ref: 61
Journal code: CE6; 9440137. ISSN: 0919-8172.
PUB. COUNTRY: Australia
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
REVIEW LITERATURE.
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011004
Last Updated on STN: 20011008
Entered Medline: 20011004
AB Progression to androgen-independence remains the main obstacle to improving survival for patients with advanced prostate cancer. In this review, findings are summarized that have recently been demonstrated to establish novel therapeutic strategy targeting several genes playing functionally important roles after androgen withdrawal and during androgen independent progression. The authors initially characterized changes in gene expression after androgen withdrawal in the androgen-dependent Shionogi and LNCaP tumor models using cDNA arrays. Based on these results, they focused on genes highly upregulated after androgen ablation (i.e. bcl-2, bcl-xL, TR.PM-2, **IGFBP-5**), which have anti-apoptotic or mitogenic activities, and thereby confer a [redacted] to cell [redacted] autologous chemotherapy. The

cancer through the inhibition of target gene expression, resulting in a delay in the progression to androgen-independence by enhancing apoptotic cell death induced by androgen ablation and chemotherapy. The authors also showed the effectiveness of combined **antisense** ODN therapy and cytotoxic chemotherapy by achieving additive or synergistic effects. These findings provide a basic significance for the design of clinical studies using **antisense** ODN either alone or in combination with chemotherapeutic agents in patients with advanced prostate cancer.

L3 ANSWER 12 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:424131 BIOSIS
DOCUMENT NUMBER: PREV200100424131
TITLE: The IGF/IGFBP system in CNS malignancy.
AUTHOR(S): Zumkeller, W. (1); Westphal, M.
CORPORATE SOURCE: (1) Department of Pediatrics, Martin-Luther-University Halle-Wittenberg, University Hospital, Ernst-Grube-Str. 40, 06097, Halle/Saale: walter.zumkeller@medizin.uni-halle.de Germany
SOURCE: Molecular Pathology, (August, 2001) Vol. 54, No. 4, pp. 227-229. print.
ISSN: 1366-8714.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The insulin-like growth factor (IGF) system includes IGF-I and IGF-II, the type I and type II IGF receptors, and specific IGF binding proteins (IGFBP-1 to IGFBP-6). These factors regulate both normal and malignant brain growth. Enhanced expression of IGF-I and IGF-II mRNA transcripts has been demonstrated in gliomas, meningiomas, and other tumours. Abnormal imprinting of IGF-II occurs in gliomas, medulloblastomas, and meningiomas. Both types of IGF receptor are expressed in gliomas and, in particular, the type I IGF receptor appears to be upregulated in malignant brain tissue. **Antisense** IGF-I receptor mRNA induces an antitumour response, resulting in complete brain tumour regression. Clinical trials for the treatment of brain tumours in humans based on a gene transfer protocol using IGF-I receptor **antisense** are under way. All six IGFBPs are expressed to a variable extent in brain tumours. High concentrations of IGFBP-2 are found in cerebrospinal fluid from patients with malignant central nervous system tumours; therefore, IGFBP-2 might be a useful marker for these tumours. IGFBP-4 appears to be a negative regulator of tumour proliferation. Both in vitro and in vivo experiments suggest that the IGF system represents an important target for the treatment of malignant central nervous system tumours and the ongoing trials should provide valuable information for future therapeutic approaches.

L3 ANSWER 13 OF 42 USPATFULL
ACCESSION NUMBER: 2001:77189 USPATFULL
TITLE: Mouse arrays and kits comprising the same
INVENTOR(S): Shchepinov, Mikhail, Palo Alto, CA, United States
Lukashev, Mathey, Newton, MA, United States
PATENT ASSIGNEE(S): Clontech Laboratories, Inc., Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
	[illegible]	[illegible]	[illegible]

on 31 Mar 1998
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Marschel, Ardin H.
LEGAL REPRESENTATIVE: Field, Bret E.Bozicevic, Field & Francis, LLP
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 1459
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Mouse arrays and methods for their use are provided. The subject arrays include a plurality of polynucleotide spots, each of which is made up of a polynucleotide probe composition of unique polynucleotides corresponding to a key mouse gene. The subject arrays find use in hybridization assays, particularly in assays for the identification of differential gene expression of key mouse genes of interest.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 14 OF 42 USPATFULL
ACCESSION NUMBER: 2000:18550 USPATFULL
TITLE: Insulin-like growth factor binding protein (IGFBP-6)
INVENTOR(S): Kiefer, Michael C., Clayton, CA, United States
Masiarz, Frank R., San Francisco, CA, United States
Zapf, Jurgen Johann Leopold, Zurich, Switzerland
Born, Walter Hans, Zurich, Switzerland
PATENT ASSIGNEE(S): Chiron Corporation, Emeryville, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6025465		20000215
APPLICATION INFO.:	US 1997-917204		19970825 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1990-576648, filed on 31 Aug 1990, now abandoned which is a division of Ser. No. US 1990-574613, filed on 28 Aug 1990, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Carlson, Karen Cochrane
LEGAL REPRESENTATIVE: Perkins & Associates, Guth, Joseph H., Blackburn, Robert P.
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 1789
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A purified binding protein selected from the group consisting of insulin-like growth factor binding protein having an amino acid sequence which is at least 75% homologous to the amino acid sequence of FIG. 1 and fragments thereof comprising at least 11 consecutive amino acids of the sequence that are capable of binding to an antibody specific for the protein or to an insulin-like growth factor is described. Recombinant DNA molecules encoding the binding proteins and subsequences thereof are also described along with recombinant microorganisms and cell lines containing the DNA molecules and methods for preparing the binding proteins by growing the recombinant hosts containing the relevant DNA molecules. Antibodies to the protein, identified as IGFBP-6, which are [illegible] described.

L3 ANSWER 15 OF 42 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 20000[redacted]0 MEDLINE
DOCUMENT NUMBER: 20310630 PubMed ID: 11051457
TITLE: Castration-induced up-regulation of **insulin-like growth factor binding protein-5** potentiates insulin-like growth factor-I activity and accelerates progression to androgen independence in prostate cancer models.
AUTHOR: Miyake H; Pollak M; Gleave M E
CORPORATE SOURCE: The Prostate Centre, Vancouver General Hospital, British Columbia, Canada.
SOURCE: CANCER RESEARCH, (2000 Jun 1) 60 (11) 3053-64.
Journal code: CNF; 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000714
Last Updated on STN: 20000714
Entered Medline: 20000621

AB Although **insulin-like growth factor binding protein-5** (**IGFBP-5**) has been shown to be implicated in prostate cancer progression, the functional role of **IGFBP-5** in progression to androgen-independence remains largely undefined. Here, we demonstrate substantial up-regulation of **IGFBP-5** during castration-induced regression and androgen-independent (AI) progression in the mouse androgen-dependent (AD) Shionogi tumor model. To analyze the functional significance of these changes in **IGFBP-5**, human AD LNCaP prostate cancer cells were stably transfected with **IGFBP-5** gene, and **IGFBP-5**-overexpressing LNCaP tumors progressed significantly faster to androgen independence after castration compared with controls. **Antisense** mouse **IGFBP-5** oligodeoxynucleotides (ODNs) were then designed that reduced **IGFBP-5** expression in Shionogi tumor cells in vitro in a dose-dependent and sequence-specific manner. Growth of Shionogi tumor cells was inhibited by **antisense IGFBP-5** ODN treatment in a time- and dose-dependent manner, which could be reversed by exogenous IGF-I. However, **antisense IGFBP-5** ODN treatment had no additive inhibitory effect on Shionogi tumor cell growth when IGF-I activity was neutralized by anti-IGF-I antibody. **Antisense IGFBP-5** ODN treatment resulted in decreased mitogen-activated protein kinase activity and number of cells in the S + G2-M phases of the cell cycle that directly correlated with reduced proliferation rate of Shionogi tumor cells. Systemic administration of **antisense IGFBP-5** ODN in mice bearing Shionogi tumors after castration significantly delayed time to progression to androgen independence and inhibited growth of AI recurrent tumors. These findings suggest that up-regulation of **IGFBP-5** after castration serves to enhance IGF bioactivity and raise the possibility that the response of prostate cancer to androgen withdrawal can be enhanced by strategies, such as **antisense IGFBP-5** ODN therapy, that target IGF signal transduction.

L3 ANSWER 16 OF 42 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 20004586[redacted] MEDLINE
DOCUMENT NUMBER: 20400567 PubMed ID: 10942528
TITLE: Increased expression of IGF-binding protein-5 in Duchenne [redacted]

AUTHOR: Melone M A; Peluso G; Galderisi U; Petillo O; Cotrufo R
CORPORATE SOURCE: Second Division of Neurology, Second University of Naples, Medical [redacted] Medicine, Naples, Italy..
marina.melone@unina2.it
SOURCE: JOURNAL OF CELLULAR PHYSIOLOGY, (2000 Oct) 185 (1) 148-53.
Journal code: HNB; 0050021. ISSN: 0021-9541.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200[illegible]
ENTRY DATE: Entered STN: 20001009
Last Updated on STN: 20001019
Entered Medline: 20000925

AB In DMD the progressive loss of muscle ability and concomitant increasing fibrosis might originate from, besides other causes, the fibroblast paracrine inhibition of satellite cell "growth." In this study we report that in myoblast/fibroblast coculture experiments, the presence of DMD fibroblasts negatively interferes with DMD myoblast growth to an extent directly proportional to the percentage of DMD fibroblasts present in the mixed-cell cultures. Moreover, the observation that media conditioned with proliferating DMD fibroblasts inhibited the growth of DMD myoblasts more seriously than did control fibroblast-conditioned media suggested a paracrine effect by diffusible factors. IGF-binding proteins could act as such diffusible factors; in fact, **IGFBP-5** transcript increased threefold in DMD fibroblasts proliferating in DMD muscle extracts, whereas IGFBP-3 mRNA decreased. In addition, high levels of **IGFBP-5** protein were detected in DMD fibroblast-conditioned media. In neutralizing **IGFBP-5** in DMD fibroblast-conditioned media by means of specific antibodies, or inhibiting **IGFBP-5** gene expression in DMD fibroblasts by means of oligo **antisense**, the fibroblast-conditioned media lost inhibitory power over DMD myoblast proliferation. Copyright 2000 Wiley-Liss, Inc.

L2 ANSWER 17 OF 42 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 20004114[illegible] MEDLINE
DOCUMENT NUMBER: 20321327 PubMed ID: 10662152
TITLE: Mesenchymal-epithelial transition in the developing metanephric kidney: gene expression study by differential display.
COMMENT: Erratum in: Genesis 2000 Jul;27(3):136
AUTHOR: Plisov S Y; Ivanov S V; Yoshino K; Dove L F; Plisova T M; Higinbotham K G; Karavanova I; Lerman M; Perantoni A O
CORPORATE SOURCE: Laboratory of Comparative Carcinogenesis, National Cancer Institute, Frederick, Maryland 21702-1201, USA..
plisov@mail.ncifcrf.gov
CONTRACT NUMBER: N01-CO-56000 (NCI)
SOURCE: GENESIS, (2000 May) 27 (1) 22-31.
Journal code: DK7; 100931242. ISSN: 1526-954X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AW672[illegible]; GENBANK-AW672[illegible]; GENBANK-AW672[illegible]; GENBANK-AW672624; GENBANK-AW672625; GENBANK-AW672626; GENBANK-AW672627; GENBANK-AW672628; GENBANK-AW672631; GENBANK-AW672633; GENBANK-AW672634; GENBANK-AW672635; GENBANK-AW672636; GENBANK-AW672637; GENBANK-AW672638; GENBANK-AW672639; GENBANK-AW672640; GENBANK-AW672641; GENBANK-AW672642; GENBANK-AW672643; GENBANK-AW672644; GENBANK-AW672645; GENBANK-AW672650; GENBANK-AW672651

Entered Medline: 20000829

AB The developing metanephric kidney is a convenient model to study molecular events associated with epithelial cell differentiation. To determine the genes involved in the defining event of this process, namely, the conversion of metanephric mesenchyme to the epithelium of the nephron, we applied differential display (DD) techniques. Explants of rat metanephric mesenchymes were induced to condense ex vivo with fibroblast growth factor 2 (FGF2) or to form tubules with FGF2 and conditioned medium (CM) from a cell line (RUB1) of ureteric bud, the renal inductive tissue. Three time points (6, 24, and 72 h) were chosen to track the dynamics of gene expression during morphogenesis. Seventy-two up- or down-regulated mRNAs were identified, including 36 novel sequences and those of cell cycle regulatory proteins (TGF-beta1, Cyclin D1, p57Kip2), transcription factors (beta-catenin, Sox11, DP1), signaling proteins (SH3-domain binding protein, G-protein-coupled receptor, Ser-Thr protein kinase), cell adhesion molecules (syndecan-4, integrin-beta1), and also gene33, H19, SM22, **IGFBP5**, MAMA receptor, lectin, keratin, beta-tubulin, calreticulin, GRP78, ERp72, Mr3cD, thioredoxin, and others. Some have previously been associated with kidney development and serve as good controls for expected changes, while most have not been linked with kidney epithelial cell differentiation. Using thin sections of embryonic kidney and labeled **antisense** RNA probes, we applied RNA hybridization to confirm the results of DD and related the expression of these genes to specific cell lineages of the developing kidney. These results provide a window into the events that mediate this critical differentiation process and suggest that a limited number of interrelated events direct the epithelial conversion of metanephric mesenchyme. genesis 27:22-31, 2000. Published 2000 Wiley-Liss, Inc.

L3 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:708627 CAPLUS
DOCUMENT NUMBER: 131:341966
TITLE: Compositions and methods for extending the action of clostridial neurotoxin and modulating neurite outgrowth in damaged neural endplates
INVENTOR(S): Dolly, J. Oliver; Acki, Kei Roger; De Paiva, Anton
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955359	A1	19991104	WO 1999-US8303	19990415
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937484	A1	19991116	AU 1999-37484	19990415
EP 1073459	A1	20010207	EP 1999-919857	19990415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

WO 1999-US8303 W 19990415

AB Methods and compns. are disclosed for modulating neurite outgrowth in damaged neural endplate. Also disclosed are methods for extending the period during which tissue treated with Clostridial toxin is paralyzed.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L3 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:421772 CAPLUS
DOCUMENT NUMBER: 131:68554
TITLE: Insulin-like growth factor binding protein fragments and their use in diagnosis and therapy
INVENTOR(S): Forssmann, Wolf-Georg; Standker, Ludger; Obendorf, Maik; Kling, Lothar; Spitz, Hans-Georg; Mostafavi, Hossein
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932620	A1	19990701	WO 1998-EP8405	19981222
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19757250	A1	19990701	DE 1997-19757250	19971222
CA 2315974	AA	19990701	CA 1998-2315974	19981222
EP 1042476	A1	20001011	EP 1998-965865	19981222
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE, IE				
JP 2002508931	T2	20020326	JP 2000-525539	19981222

PRIORITY APPLN. INFO.: DE 1997-19757250 A 19971222
WO 1998-EP8405 W 19981222

OTHER SOURCE(S): MARPAT 131:68554

AB The invention relates to peptides which are derived from insulin-like growth factor binding protein (IGFBP). The invention also relates to cyclic, glycosylated, phosphorylated, acetylated, amidated and/or sulfatized derivs. of these peptides. The peptides may be isolated from hemofiltrate or urine. Thus, an IGFBP-2 fragment was isolated from hemofiltrate and this peptide complexed with IGF was shown to have a neuroprotective effect on PC-12 cells. In addn., an IGFBP-4 fragment was found to stimulate proliferation of osteoblasts.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L3 ANSWER 20 OF 42 USPATFULL
ACCESSION NUMBER: 1999:106316 USPATFULL
TITLE: TNF receptor death domain ligand protein
INVENTOR(S): Lin, Lih-ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schievella, Andrea R., Winchester, MA, United States
Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5948638		19990907

continuation-in-part of Ser. No. US 1995-494440, filed on [redacted] Jun 1995, now patented, Pat. No. US 5849501 which

is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Feisee, Lila
ASSISTANT EXAMINER: Kaufman, Claire M.
LEGAL REPRESENTATIVE: Sprunger, Suzanne A., Brown, Scott A.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s) ; 8 Drawing Page(s)
LINE COUNT: 3130
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing the TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 11 OF 42 USPATFULL
ACCESSION NUMBER: 1999:43423 USPATFULL
TITLE: TNF receptor death domain ligand proteins
INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schievella, Andrea R., Winchester, MA, United States
Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5891675		19990406
APPLICATION INFO.:	US 1997-838032		19970413 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1996-698551, filed on 15 Aug 1996, now patented, Pat. No. US 5712381, issued on 27 Jan 1998 which is a continuation-in-part of Ser. No. US 1996-601226, filed on 15 Feb 1996 which is a continuation-in-part of Ser. No. US 1995-533901, filed on 26 Sep 1995 which is a continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kim, John
LEGAL REPRESENTATIVE: Sprunger, Suzanne A., Brown, Scott A.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 2439
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are [illegible] and methods of making

TNF-R1-TD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 22 OF 42 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999357922 MEDLINE
DOCUMENT NUMBER: 99357922 PubMed ID: 10427145
TITLE: Inhibition of insulin-like growth factor I receptor signaling by the vitamin D analogue EB1089 in MCF-7 breast cancer cells: A role for insulin-like growth factor binding proteins.
AUTHOR: Rozen F; Pollak M
CORPORATE SOURCE: Lady Davis Institute for Medical Research of the Jewish General Hospital and Departments of Medicine and Oncology, McGill University, Montreal, Quebec H3T 1E2, Canada.
SOURCE: INTERNATIONAL JOURNAL OF ONCOLOGY, (1999 Sep) 15 (3) 589-94.
Journal code: CX5; 9306042. ISSN: 1019-6439.
PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 20000303
Entered Medline: 19991014

AB Insulin-like growth factors I and II (IGF-I and IGF-II) are potent mitogens involved in growth regulation of breast epithelial cells and are implicated in the pathophysiology of breast cancer. Their bioactivity is enhanced or inhibited by specific IGF-binding proteins (IGFBPs). Vitamin D-related compounds (VDRCs) have been shown to inhibit proliferation and induce apoptosis of MCF-7 breast carcinoma cells. We have previously demonstrated that VDRCs antagonize the growth-promoting activity of IGF-I by stimulating autocrine production of **IGFBP-5** in MCF-7 cells, but the effect of VDRCs on IGF-I receptor (IGF-IR) intracellular signaling has not been elucidated. We report here that the vitamin D analogue EB1089 interferes with the IGF-IR signaling pathway by attenuating IGF-I-induced tyrosine phosphorylation of IRS-1, and to a lesser extent, IRS-2. It does not affect protein levels of IRS-1, IRS-2 or IGF-IR. However, EB1089 does not inhibit tyrosine phosphorylation of IRS-1 induced by des(1-3) IGF-I, an IGF-I analogue with greatly reduced affinity for IGFBPs. Furthermore, we demonstrate that an **antisense IGFBP-5** oligodeoxynucleotide attenuates EB1089-induced inhibition of IGF-I-stimulated tyrosine phosphorylation of IRS-1 and EB1089-induced **IGFBP-5** accumulation. These data strongly suggest that **IGFBP-5** plays a functional role in the interfering action of EB1089 with the IGF-IR signal transduction pathway.

L3 ANSWER 23 OF 42 USPATFULL
ACCESSION NUMBER: 1998:160103 USPATFULL
TITLE: TNF receptor death ligand proteins and inhibitors of ligand binding
INVENTOR(S): Lin, Lih-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Schwenzer, Andrew R., Winchester, MA, United States

(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5852178		19981222
APPLICATION INFO.:	US 1995-[illegible]		19950926 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Walsh, Stephen		
ASSISTANT EXAMINER:	Kaufman, Claire M.		
LEGAL REPRESENTATIVE:	Sprunger, Suzanne A., Brown, Scott A., DesRosier, Thomas J.		
NUMBER OF CLAIMS:	7		
EXEMPLARY CLAIM:	7		
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 8 Drawing Page(s)		
LINE COUNT:	1955		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing the TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 24 OF 42 USPATFULL

ACCESSION NUMBER:	1998:157114 USPATFULL
TITLE:	TNF receptor death domain ligand proteins and method to identify inhibitors of ligand binding
INVENTOR(S):	Lin, Lin-Ling, Concord, MA, United States Chen, Jennifer, Chestnut Hill, MA, United States Schievella, Andrea R., Winchester, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5843501		19981215
APPLICATION INFO.:	US 1995-494440		19950619 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Walsh, Stephen		
ASSISTANT EXAMINER:	Kaufman, Claire M.		
LEGAL REPRESENTATIVE:	Brown, Scott A., Sprunger, Suzanne A., DesRosier, Thomas J.		
NUMBER OF CLAIMS:	6		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 6 Drawing Page(s)		
LINE COUNT:	1627		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1 DD") ligand proteins are [illegible] TNF-R1 DD ligand protein are

TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 25 OF 42 USPATFULL

ACCESSION NUMBER:	1998:154394 USPATFULL
TITLE:	TNF receptor death domain ligand proteins
INVENTOR(S):	Lin, Lih-Ling, Concord, MA, United States Chen, Jennifer, Chestnut Hill, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5847099		19981208
APPLICATION INFO.:	US 1996-643341		19960517 (3)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Walsh, Stephen		
ASSISTANT EXAMINER:	Kaufman, Claire M.		
LEGAL REPRESENTATIVE:	Brown, Scott A., DesRosier, Thomas J.		
NUMBER OF CLAIMS:	15		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Figure(s); 2 Drawing Page(s)		
LINE COUNT:	1343		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing the TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 26 OF 42 USPATFULL

ACCESSION NUMBER:	1998:150691 USPATFULL
TITLE:	TNF receptor death domain ligand proteins and inhibitors of ligand binding
INVENTOR(S):	Lin, Lih-Ling, Concord, MA, United States Chen, Jennifer, Chestnut Hill, MA, United States Schievella, Andrea R., Winchester, MA, United States Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5841675		19981201
APPLICATION INFO.:	US 1996-602228		19960215 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-533901, filed on 26 Sep 1995 which is a continuation-in-part of Ser. No. US 1995-494447, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed

FILE SEGMENT: Granted
PRIMARY EXAMINER: Ulm[redacted]John
LEGAL REPRESENTATIVE: Sp[redacted]er, Suzanne A., Brown, Scott A[redacted]
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 6
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1129
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1-DD ligand protein. Pharmaceutical compositions containing the TNF R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 27 OF 42 USPATFULL
ACCESSION NUMBER: 1998:45043 USPATFULL
TITLE: Methods and reagents for the identification and regulation of senescence-related genes
INVENTOR(S): Linskens, Maarten H. K., Palo Alto, CA, United States
Hirsch, Kenneth S., Palo Alto, CA, United States
Villeponteau, Bryant, San Carlos, CA, United States
Feng, Junli, San Carlos, CA, United States
Funk, Walter, Union City, CA, United States
West, Michael David, Belmont, CA, United States
PATENT ASSIGNEE(S): Geron Corporation, Menlo Park, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5744300		19980428
APPLICATION INFO.:	US 1994-332420		19941031 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-235180, filed on 29 Apr 1994, now patented, Pat. No. US 5580726 And Ser. No. US 1993-35766, filed on 24 Mar 1993, now patented, Pat. No. US 5489508		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Myers, Carla J.
LEGAL REPRESENTATIVE: Kaster, KevinLyon & Lyon LLP
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 2405
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Identification of senescence-related genes can be accomplished by comparing mRNA expression between young and senescent cells. Probes complementary to such genes can be used to detect senescent cells and distinguish between young and senescent cells as well as in screens to identify compounds that alter expression levels of senescence related genes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 28 OF 42 USPATFULL
ACCESSION NUMBER: 1998:9502 USPATFULL
TITLE: MAFF, a TNF receptor death domain ligand protein
INVENTOR(S): Lin, Lih Ling, Concord, MA, United States
[redacted], Framingham, MA, United States

PATENT ASSIGNEE(S) : Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5711938		19980127
APPLICATION INFO.:	US 1996-644551		19960815 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-602228, filed on 15 Feb 1996 which is a continuation-in-part of Ser. No. US 1995-538301, filed on 26 Sep 1995 which is a continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Walsh, Stephen
ASSISTANT EXAMINER: Ranjan, Mukul
LEGAL REPRESENTATIVE: Brown, Scott A., Sprunger, Suzanne A., DesRosier, Thomas J.
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1329
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel TNF receptor death domain ("TNF-R1-DD") ligand proteins are disclosed. Polynucleotides encoding the TNF-R1-DD ligand protein are also disclosed, along with vectors, host cells, and methods of making the TNF-R1 DD ligand protein. Pharmaceutical compositions containing the TNF-R1-DD ligand protein, methods of treating inflammatory conditions, and methods of inhibiting TNF-R death domain binding are also disclosed.

Methods of identifying inhibitors of TNF-R death domain binding and inhibitors identified by such methods are also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 29 OF 42 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 1998187774 MEDLINE
DOCUMENT NUMBER: 98187774 PubMed ID: 9528925
TITLE: Up-regulation of **insulin-like growth factor binding protein-5** is independent of muscle cell differentiation, sensitive to rapamycin, but insensitive to wortmannin and LY294002.
AUTHOR: Rousse S; Montarras D; Pinset C; Dubois C
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale, U.148, Hopital Saint Antoine, Paris, France.
SOURCE: ENDOCRINOLOGY, (1998 Apr) 139 (4) 1487-93.
Journal code: EGZ; 1370040. ISSN: 0013-7227.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980414
Last Updated on STN: 20000303
Entered Medline: 19980414

AB Skeletal myoblast differentiation is stimulated by insulin-like growth factors (IGFs). The autocrine action of IGFs is mediated through the type-1 IGF receptor (IGFR-1) and modulated by IGF binding proteins [illegible] myoblast cell line stably

cells: high levels of IGFBP-2 messenger RNA (mRNA) were found only in proliferating myoblast[redacted] whereas IGFBP-5 mRNA was induced in quiescent cells. Secretion of **IGF[redacted]5** was strongly stimulated duri[redacted] differentiation. Insulin and IGF dose-response experiments showed that up-regulation of **IGFBP-5** resulted from IGFR-1 activation. Drugs interfering with IGFR-1 signaling and inhibiting myoblast differentiation had different effects on **IGFBP-5** up-regulation. Two phosphatidylinositol 3-kinase (PI 3-kinase) inhibitors, wortmannin and LY294002 [2- (4-morpholinyl)-8-phenyl-4H-1-benzopyran-4-one], failed to alter **IGFBP-5** up-regulation, which persisted in the absence of differentiation. Rapamycin which indirectly prevents activation of the p70 ribosomal protein-S6 kinase (p70S6k), suppressed **IGFBP-5** induction. Because the PI3-kinase inhibitors block p70S6k, neither kinase would be required for IGFR-1 dependent **IGFBP-5** induction. In C2 anti IGF-II myoblasts, **IGFBP-5** induction is therefore rapamycin-sensitive and independent of differentiation.

L3 ANSWER 30 OF 42 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 1999099111 MEDLINE
DOCUMENT NUMBER: 99099111 PubMed ID: 9879061
TITLE: Differential expression and localization of IGF-I and IGF binding proteins in inflamed rat colon.
AUTHOR: Zeen J M; Mohapatra N; Lund P K; Eysselein V E; McRoberts J
A
CORPORATE SOURCE: Harbor UCLA Medical Center, Division of Gastroenterology, Torrance, CA, USA.
CONTRACT NUMBER: DK34987 (NIDDK)
DK42274 (NIDDK)
DK47769 (NIDDK)
SOURCE: JOURNAL OF RECEPTOR AND SIGNAL TRANSDUCTION RESEARCH, (1998
Jul-Nov) 18 (4-6) 265-80.
Journal code: CCU; 9509432. ISSN: 1079-9893.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990311

AB Recent studies indicate increased insulin-like growth factor I (IGF-I) expression and altered expression of IGF binding proteins (IGFBP) in the bowel during experimental colitis. This study analyzes the cellular sites of altered IGF-I and IGFBP-expression in large bowel of rats with experimental colitis. Colitis was induced by colonic instillation of 2, 4,
6-trinitrobenzenesulfinic (TNB) acid in ethanol. Animals were sacrificed at 7 days after induction of colitis. Cryostat sections of colon from TNB-treated and control rats were hybridized with ^{35}S-labeled **antisense** probes for IGF-I, IGFBP-3, IGFBP-4 and **IGFBP-5**. IGF I mRNA was up regulated in lamina propria cells, submucosa and smooth muscle of inflamed colon. IGFBP-3 mRNA was localized to lamina propria and was down-regulated in inflamed colon. IGFBP-4 and **IGFBP-5** mRNAs were both up-regulated in inflamed colon. IGFBP-4 mRNA was increased in lamina propria, submucosa and smooth muscle, whereas **IGFBP-5** mRNA was increased in smooth muscle. Increased IGF-I expression in mesenchymal layers of colon during experimental colitis supports the hypothesis that IGF-I contributes to [redacted] Altered expression

action.

L3 ANSWER 31 OF 42 MEDLINE
ACCESSION NUMBER: 97278858 MEDLINE
DOCUMENT NUMBER: 97278858 PubMed ID: 9133435
TITLE: Insulin-like growth factor binding protein gene expression in the pregnant rat uterus and placenta.
AUTHOR: Ferro J A; Pintar J E
CORPORATE SOURCE: Department of Anatomy and Cell Biology, Columbia University
College of Physicians and Surgeons, New York, New York 10032, USA.
CONTRACT NUMBER: NS21970 (NINDS)
SOURCE: DEVELOPMENTAL BIOLOGY, (1997 Apr 15) 184 (2) 278-95.
Journal code: E7T; 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19970612
Entered Medline: 19970602

AB While the insulin-like growth factor (IGF) system plays a fundamental role in regulating embryonic and placental growth, the specific contributions of the six IGF binding proteins (IGFBPs 1-6) to these processes are not well understood. We here focus on IGFBP expression in the extraembryonic environment, which both supports and constrains embryonic growth, and have used in situ hybridization to determine sites of IGFBP mRNA synthesis in the pregnant rat uterus and placenta. We find that all IGFBPs are expressed in distinct, changing patterns in the uterine endometrium, at the decidual boundary, in the decidual vasculature, and in the myometrium during pregnancy. Within the endometrium, the most prominent change is that expression of IGFBP-1 begins in some, but not all, endometrial glands prior to implantation and then expands to include all secretory epithelia shortly after implantation. During the period of rapid decidual proliferation that follows implantation, IGFBP-3, -4, and -5 transcripts are all detected in a laminar array at the boundary between the decidua and the nondecidualized endometrium. In the decidual vasculature at Day (d) 8.0, both IGFBP-3 and IGFBP-4 mRNAs are detected in dilating blood vessels, with BP-3 most prominent in the antimesometrial plexus and BP-4 primarily at the mesometrial pole. Later (d11.5), all decidual vessels express high levels of IGFBP-3 and lower levels of IGFBP-4 mRNAs. Finally, changes in expression of several IGFBPs also occur within the myometrium during pregnancy. For example, IGFBP-2 is expressed in the inner circular layer shortly after implantation, and expression increases through late gestation. In contrast, **IGFBP-5** hybridization occurs over both myometrial layers before implantation, but decreases in intensity and spatial distribution as pregnancy proceeds. Finally, and most strikingly, IGFBP-6 expression, barely detectable in the d7.5 myometrium, gradually increases until it is very strongly transcribed during the placental stages. Taken together, these observations suggest multiple roles for IGFBPs in supporting implantation, regulating the extent of decidualization, modulating local levels of vascular IGFs, and regulating uterine muscular growth.

L3 ANSWER 32 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:372693 BIOSIS
DOCUMENT NUMBER: PREV199799672193
In vitro and in vivo studies on the role of insulin-like

AUTHOR(S): Kanzaki, S. (1); Mohan, S.; Ono, T. (1); Matsuoka, Y. (1); Moriwaki, T. (1); Tanaka, H. (1); Seino, [redacted] (1)

CORPORATE SOURCE: (1) Dept. Pediatrics, Okayama Univ. Med. [redacted]., Okayama 700 Japan.

SOURCE: Hormone Research (Basel), (1997) Vol. 48, No. SUPPL. 2, pp. 16.
Meeting Info.: 5th Joint Meeting of the European Society for Paediatric Endocrinology and the Lawson Wilkins Society for Pediatric Endocrinology, in Collaboration with the Australian Paediatric Endocrine Group, the Japanese Society for Pediatric Endocrinology and the Latin American Society for Paediatric Endocrinology Stockholm, Sweden June 22-26, 1997
ISSN: 0301-0163.

DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English

L? ANSWER 33 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:211609 CAPLUS
DOCUMENT NUMBER: 124:270941
TITLE: Use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment of proliferative and/or inflammatory skin disorders
INVENTOR(S): Werther, George Arthur; Wraight, Christopher John
PATENT ASSIGNEE(S): Royal Children's Hospital Research Foundation, Australia
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9601636	A1	19960125	WO 1995-AU410	19950706
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2194366	AA	19960125	CA 1995-2194366	19950706
AU 9528753	A1	19960209	AU 1995-28753	19950706
AU 692278	B2	19980604		
EP 776210	A1	19970604	EP 1995-924110	19950706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP [redacted]	T2	1998[redacted]19	JP 1995-504113	19950706
US [redacted]	A	19980[redacted]20	US 1996-666382	19960820
US 6[redacted]	B1	20010[redacted]04	US 1998-[redacted]	19981123

PRIORITY APPLN. INFO.: AU 1994-67105 A 19940708
WO 1995-AU410 W 19950706
US 1996-666382 A1 19960820

AB The present invention relates generally to a method for the prophylaxis and/or treatment of skin disorders, and in particular proliferative and/or inflammatory skin disorders, and to nucleic acids or nucleic acid analogs [redacted]

stimulation of this layer of cells. The present invention contemplates, in a most preferred embodiment, a method for the prophylaxis and/or treatment of psoriasis. Phosphorothioate-linked oligonucleotide (18- and 24-mers) **antisense** to human insulin-like growth factor binding protein 3-encoding nucleic acid inhibited IGFBP-3 synthesis by HaCaT cells
human differentiated keratinocyte cell line).

L3 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 8
ACCESSION NUMBER: 1996:254013 CAPLUS
DOCUMENT NUMBER: 124:308419
TITLE: Osteogenic protein-1-mediated insulin-like growth factor gene expression in primary cultures of rat osteoblastic cells
AUTHOR(S): Yeh, Lee-Chuan C.; Adamo, Martin L.; Ritten, Allison M.; Olson, Merle S.; Lee, John C.
CORPORATE SOURCE: Department Biochemistry, University Texas Health Science Center, San Antonio, TX, 78284-7760, USA
SOURCE: Endocrinology (1996), 137(5), 1821-31
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Osteogenic protein-1 (OP-1) is a member of the bone morphogenetic protein family and has been shown to induce new bone formation in vivo. In the present study, the authors detd. whether the expression of the IGF system,
a significant growth factor system in bone, was altered by OP-1 in primary
cultures of fetal rats calvarial cells. Levels of mRNA encoding insulin-like growth factor I (IGF-I, IGF-II, IGF-I receptor, and IGF-binding proteins (IGFBP-1)+ mRNA was elevated in an OP-1 concn. (0-1000 ng/mL)-dependent manner, with maximal stimulation of IGF-I mRNA of
2- to 3-fold apparent 24 h after treatment. The increase in the IGF-I mRNA level involved a preferential stimulation of transcripts initiated at
start site 2 in the exon 1 promoter. The level of IGF-II mRNA also increased by approx. 2-fold in OP-1-treated cells in a concn.-dependent manner. The level of IGF-I receptor mRNA was not altered by treatment. Whereas IGFBP-1 mRNA was not detected in these cells, IGFBP-2 mRNA was expressed, but the expression was not changed after treatment for 48 h in the concn. range (0-1000 ng/mL) tested. The IGFBP-2 mRNA level was increased slightly 48 h after OP-1 treatment in a concn.-dependent manner.
The IGFBP-4, -5, and -6 mRNA levels decreased dramatically in an OP-1 concn.-dependent manner. In addn., coincubation of **antisense** oligonucleotides corresponding to IGF-I or -II mRNA sequence with OP-1 reduced the OP-1-induced elevation in alk. phosphatase activity. The present results suggest that the differentiation of rat osteoblastic cells
in response to OP-1 is mediated in part by increased IGF-I and -II gene expression and alterations in the gene expression of different IGFBPs.

L3 ANSWER 35 OF 42 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 97084055 MEDLINE
DOCUMENT NUMBER: 97084055 PubMed ID: 8930999
TITLE: A role for **insulin like growth factor binding protein 5** in the antiproliferative action of the antiestrogen ICI 182780.
AUTHOR: Huynh H; Yang X F; Pollak M
CORPORATE SOURCE: Lady Davis Research Institute, Jewish General Hospital, Montreal, Quebec, Canada.
[illegible] GROWTH AND DIFFERENTIATION, 1996 May 7 [illegible].

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970306
Last Updated on STN: 19970306
Entered Medline: 19970227

AB Insulin-like growth factors (IGFs) are potent mitogens for breast cancer cells. Although IGF-binding proteins (IGFBPs) are known to regulate access of IGFs to IGF receptors, their precise biological actions are poorly defined. We observed that the potent antiestrogen ICI 182780 (ICI) increased **IGFBP-5** mRNA by 2- to 5-fold in 9,10-dimethyl-1,2-benzanthracene-induced mammary tumors in vivo. In vitro studies showed that growth inhibition of MCF-7 human breast cancer cells induced by ICI was associated with increased transcription of the **IGFBP-5** gene, increased **IGFBP-5** mRNA abundance, and increased **IGFBP-5** protein accumulation in the conditioned medium. Growth stimulation following estradiol exposure was associated with opposite effects. An **IGFBP-5** **antisense** oligodeoxynucleotide significantly decreased **IGFBP-5** accumulation in conditioned media and enhanced MCF-7 cell DNA synthesis. Furthermore, this **antisense** oligodeoxynucleotide attenuated both antiestrogen-induced **IGFBP-5** accumulation and antiestrogen-induced growth inhibition. These data demonstrate that estradiol down-regulates and ICI up-regulates an autocrine **IGFBP-5** growth inhibitory pathway in MCF-7 cells and suggest that **IGFBP-5** plays a role in modulation of proliferation of breast cancers by estrogens and antiestrogens.

L3 ANSWER 36 OF 42 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 96245221 MEDLINE
DOCUMENT NUMBER: 96245221 PubMed ID: 8641849
TITLE: Localization of mRNAs for insulin-like growth factor-I (IGF-I), IGF-I receptor, and IGF binding proteins in rat eye.
AUTHOR: Burren C P; Berka J L; Edmondson S R; Werther G A; Batch J A
CORPORATE SOURCE: Centre for Hormone Research, Royal Children's Hospital, Parkville, Victoria, Australia.
SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1996 Jun) 37 (7) 1459-68.
Journal code: GWI; 7703701. ISSN: 0146-0404.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960726
Last Updated on STN: 20000303
Entered Medline: 19960716

AB PURPOSE. To localize mRNAs for insulin-like growth factor (IGF) I, IGF-I receptor (IGF-IR), and IGF binding protein (IGFBP) 1 to IGFBP-6 in the rat eye. METHODS. cDNA sequences for IGF-I, IGF-IR, and IGFBP-1 to IGFBP-6 were used to synthesize ^{35}S-UTP labeled **antisense** and sense probes for in situ hybridization on 5-microns sections of the rat eye, including the retina, choroid, sclera, ciliary body, and cornea. RESULTS. IGF-I mRNA was demonstrated over ganglion cells of the retina and endothelial cells of the choroid and ciliary processes. IGF-IR mRNA showed more extensive distribution, localizing to the retinal ganglion cell [illegible]

and lens. IGFBP-. mRNA localized to outer nonpigmented epithelia of the ciliary processes and [redacted] germinal layer of corneal epithelium as well as iris, conjunctiva, and sclera. Messenger RNAs for IGFBP [redacted] to IGFBP-6 localized to choroidal endothelial cells and chromatophores and also to the inner pigmented epithelium of the ciliary processes. Messenger RNAs for **IGFBP-5** and IGFBP-6 were seen in the inner and outer nuclear layers of the neural retina. IGFBP-1 mRNA was not detected within the rat eye. CONCLUSIONS. Using in situ hybridization, we have demonstrated mRNAs for IGF-I, IGF-II, and IGFBP-3 to IGFBP-6 in specific histologic layers of the retina, choroid, ciliary body, and cornea in the rat. The characterization of the IGF system in vivo suggests specific roles in the normal eye and provides a basis for studying the IGF system in eye pathology.

L3 ANSWER 37 OF 40 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 96222370 MEDLINE
DOCUMENT NUMBER: 96222370 PubMed ID: 8636241
TITLE: **Insulin-like growth factor binding protein-5** modulates muscle differentiation through an insulin-like growth factor-dependent mechanism.
AUTHOR: James I L; Stewart C E; Rotwein P
CORPORATE SOURCE: Department of Biochemistry, Washington University, School of Medicine, St. Louis, Missouri 63110, USA.
CONTRACT NUMBER: 5R01 DK46748 (NIDDK)
DK-0579 (NIDDK)
SOURCE: JOURNAL OF CELL BIOLOGY, (1996 May) 133 (3) 683-93.
Journal code: HMV; 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 19960719
Last Updated on STN: 19960719
Entered Medline: 19960711

AB The insulin-like growth factor binding proteins (IGFBPs) are a family of six secreted proteins which bind to and modulate the actions of insulin-like growth factors-I and -II (IGF-I and -II). **IGFBP-5** is more conserved than other IGFBPs characterized to date, and is expressed in adult rodent muscle and in the developing myotome. We have shown previously that C2 myoblasts secrete **IGFBP-5** as their sole IGFBP. Here we use these cells to study the function of **IGFBP-5** during myogenesis, a process stimulated by IGFs. We stably transfected C2 cells with **IGFBP-5** cDNAs under control of a constitutively active promoter. Compared with vector-transfected control cells, C2 myoblasts expressing the **IGFBP-5** transgene in the sense orientation exhibit increased **IGFBP-5** levels in the extracellular matrix during proliferation, and subsequently fail to differentiate normally, as assessed by both morphological and biochemical criteria. Compared to controls, **IGFBP-5** sense myoblasts show enhanced survival in low serum medium, remaining viable for at least four weeks in culture. By contrast, myoblasts expressing the **IGFBP 5 antisense** transcript differentiate prematurely and more extensively than control cells. The inhibition of myogenic differentiation by high level expression of **IGFBP-5** could be overcome by exogenous IGFs, with des (1-3) IGF-I, an analogue with decreased affinity for **IGFBP-5** but normal affinity for the IGF-I receptor, showing the highest potency. These results are consistent with a model in which **IGFBP-5** blocks IGF stimulated

suggest that **IGFBP-5** normally inhibits muscle differentiation, and [illegible]y a role for **IGFBP-5** in regulating IGF action during myogenic development in vi[illegible]

L9 ANSWER 39 OF 49 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 97052388 MEDLINE
DOCUMENT NUMBER: 97052388 PubMed ID: 8997702
TITLE: Growth hormone and the insulin-like growth factor system in myogenesis.
AUTHOR: Florini J R; Ewton D Z; Coolican S A
CORPORATE SOURCE: Biology Department, Syracuse University, New York 13244, USA.
CONTRACT NUMBER: HL11551 (NHLBI)
SOURCE: ENDOCRINE REVIEWS, (1996 Jun) 17 (5) 481-517. Ref: 465
Journal code: EIR; 8005253. ISSN: 0163-769X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 19970227
Entered Medline: 19970211

AB It is very clear that the GH-IGF axis plays a major role in controlling the growth and differentiation of skeletal muscles, as it does virtually all of the tissues in the animal body. One aspect of this control is unquestioned: circulating GH acts on the liver to stimulate expression of the IGF-I and IGFBP3 genes, substantially increasing the levels of these proteins in the circulation. It also seems that GH stimulates expression of IGF-I genes in skeletal muscle, although there are a number of cases in which skeletal muscle IGF-I expression is elevated in the absence of GH. It is substantially less clear that GH acts directly on skeletal muscle to stimulate its growth; the presence of GH receptor mRNA in skeletal muscle is well established, but most investigators have been unsuccessful in demonstrating any specific binding of GH to skeletal muscle or to myoblasts in culture. It has been equally difficult to show direct actions of GH on cultured muscle cells; the only positive report concludes that the early insulin-like effects of GH can result from direct interactions between GH and isolated muscle cells. The effects of the IGFs on skeletal muscle are much clearer. It is well established by studies in a number of laboratories on a variety of systems that IGFs stimulate many anabolic responses in myoblasts, as they do in other cell types. IGFs have the unusual property of stimulating both proliferation and differentiation of myoblasts, responses that are generally believed to be mutually exclusive; in myoblasts, they are in fact temporally separated. The stimulation of differentiation by IGF-I is (at least in part) a result of substantially increased levels of the mRNA for myogenin, the member of the MyoD family most directly associated with terminal myogenesis. As levels of myogenin mRNA rise, those of myf-5 mRNA (the only other member of the MyoD family expressed significantly in L6 myoblasts) fall dramatically, although myf-5 expression is required for the initial elevation of myogenin. The effects of IGFs are significantly modulated by IGFBPs secreted by myoblasts in serum-free medium, inhibitory IGFBPs-4 and -6 are expressed and secreted by L6A1 myoblasts, while expression of **IGFBP-5** rises dramatically as differentiation proceeds. Other myoblasts also secrete [illegible] Some of exogenous IGFs are not added to the low-serum

myogenic cell lines, such as Sol 8, are so active in expressing the IGF-II gene that it is not possible to demonstrate effects of exogenous IGFs. This autocrine expression of IGFs is by no means unique to skeletal muscle cells; indeed, it is so widely seen in cells responding to mitogenic stimuli that we suggest that IGFs can be viewed as extracellular second messengers that mediate most, if not all, such actions of agents that stimulate cell proliferation. The component of serum that suppresses IGF-II gene expression under "growth" conditions appears to be the IGFs themselves, which exhibit a very high potency in the feedback inhibition of IGF-II expression. In addition, IGFs have effects on the expression of other genes related to differentiation. Treatment of L6A1 cell with IGFs suppresses their expression of the myogenesis-inhibiting TGF beta s with a time course consistent with an initial proliferative step followed by differentiation, i.e. expression is first increased and then very substantially decreased. It is not established that this plays a role in control of differentiation, but experiments with FGF **antisense** constructs suggests that this may well be the case. Until recently, IGFs were the only circulating agents known to stimulate myoblast differentiation, in contrast to the relatively large number of growth factors that inhibit the process. It is now clear that thyroid hormones and RA also stimulate myogenesis, and that IL-15 enhances the stimulatory eff

L3 ANSWER 39 OF 43 MEDLINE DUPLICATE 13
ACCESSION NUMBER: 96109186 MEDLINE
DOCUMENT NUMBER: 96109186 PubMed ID: 8613825
TITLE: Insulin-like growth factor II mediates epidermal growth factor-induced mitogenesis in cervical cancer cells.
AUTHOR: Steller M A; Delgado C H; Zou Z
CORPORATE SOURCE: Section of Gynecologic Oncology, National Cancer Institute, Bethesda, MD 20892-1500, USA.
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Dec 19) 92 (26) 11970-4. Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English.
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 19960620
Last Updated on STN: 20000303
Entered Medline: 19960607

AB There is increasing evidence that activation of the insulin-like growth factor I (IGF-I) receptor plays a major role in the control of cellular proliferation of many cell types. We studied the mitogenic effects of IGF-I, IGF-II, and epidermal growth factor (EGF) on growth-arrested HT-3 cells, a human cervical cancer cell line. All three growth factors promoted dose-dependent increases in cell proliferation. In untransformed cells, EGF usually requires stimulation by a "progression" factor such as IGF-I, IGF-II, or insulin in supraphysiologic concentrations in order to exert a mitogenic effect. Accordingly, we investigated whether an autocrine pathway involving IGF-I or IGF-II participated in the EGF-induced mitogenesis of HT-3 cells. With the RNase protection assay, IGF-I mRNA was not detected. However, IGF-II mRNA increased in a time-dependent manner following EGF stimulation. The EGF-induced mitogenesis was abrogated in a dose-dependent manner by IGF-binding protein 5 (**IGFBP-5**), which binds to IGF-II and neutralizes it. An **antisense** oligonucleotide to IGF-II also inhibited the proliferative response to EGF. In addition, prolonged, but not short-term, stimulation with EGF resulted in autophosphorylation of

secretion of IGF-II in HT-3 cervical cancer cells can participate in EGF-induced mitogenesis and suggest that autocrine signals involving the IGF-I receptor occur "downstream" of competence growth factor receptors such as the EGF receptor.

L3 ANSWER 40 OF 42 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 96082466 MEDLINE
DOCUMENT NUMBER: 96082466 PubMed ID: 7476972
TITLE: Regulation of insulin-like growth factor (IGF)-binding protein-6 and mannose 6-phosphate/IGF-II receptor expression in IGF-II-overexpressing NIH 3T3 cells.
AUTHOR: Claussen M; Buergisser D; Schuller A G; Matzner U; Braulke T
CORPORATE SOURCE: Institute for Biochemistry II, University of Gottingen, Germany.
SOURCE: MOLECULAR ENDOCRINOLOGY, (1995 Jul) 9 (7) 802-10.
Journal code: MSZ; 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 20001003
Entered Medline: 19951212

AB Insulin-like growth factor II (IGF-II)-overexpressing NIH 3T3 cells were used to examine regulation of insulin-like growth factor binding protein (IGFBP) and mannose 6-phosphate (M6P)/IGF-II receptor expression. Ligand blot analysis of conditioned media indicated a predominant IGFBP of 26-28 kilodaltons the abundance of which is 5- to 10-fold higher in media of IGF-II-overexpressing cells. The IGFBP level in control cell medium was increased by incubation in the presence of IGF-II, IGF-I, and mutant IGF-II forms with reduced affinities for IGF-I or M6P/IGF-II receptors. Further proof that IGF-II regulated the IGFBP was obtained by incubation of IGF-II overexpressing cells in the presence of **antisense** IGF-II oligomers or anti-IGF-II antibodies, which resulted in significant reduction of the IGFBP in conditioned medium. Mouse IGFBP-6 mRNA expression was increased in IGF-II-overexpressing or IGF-II-treated control cells. The IGFBP contained O-linked carbohydrate residues and was recognized by an antiserum to rat IGFBP-6. To determine whether IGFs were influencing proteolytic degradation of IGFBPs, cell-free conditioned media were incubated at 37 C with recombinant human IGFBPs. At neutral pH proteolysis of **IGFBP-5** occurred during incubation in conditioned media from control and IGF-II-overexpressing cells. Upon acidification of the medium samples, only the degradation of IGFBP-6 was prevented in IGF-II-overexpressing cell-conditioned medium.(ABSTRACT TRUNCATED AT 250 WORDS)

L3 ANSWER 41 OF 42 MEDLINE DUPLICATE 15
ACCESSION NUMBER: 94259769 MEDLINE
DOCUMENT NUMBER: 94259769 PubMed ID: 7515389
TITLE: Expression of the genes encoding the insulin-like growth factors (IGF-I and II), the IGF and insulin receptors, and IGF binding proteins-1-6 and the localization of their gene products in normal and polycystic ovary syndrome ovaries.
AUTHOR: el-Roeiy A; Chen X; Roberts V J; Shimasaki S; Ling N; LeRoith D; Roberts C T Jr; Yen S S
CORPORATE SOURCE: Department of Reproductive Medicine, University of California School of Medicine, La Jolla 92093.
CONTRACT NUMBER: HD-07203-10 (NICHD)
HD-07213-11 (NICHD)

Journal Code: HRB; 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
Journal; Article; JOURNAL ARTICLE
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940714
Last Updated on STN: 20000303
Entered Medline: 19940705

AB To discern the potential role of the insulin-like growth factors (IGFs) in polycystic ovary syndrome (PCOS), we examined the expression of the genes encoding the IGFs, IGF receptors (IGFr), insulin receptor (Ir), and IGF-binding proteins (IGFBPs-1-6) as well as the localization of the gene products in specific cellular compartments of normal and PCOS human ovaries. Messenger ribonucleic acid (mRNA) was localized by in situ hybridization with specific 35S-labeled human **antisense** RNA probes, and protein was detected by immunohistochemistry using specific antisera. Thecal cells, but not granulosa cells (GC), of small antral follicles (3-6 mm) from PCOS ovaries expressed both IGF-I and IGF-II transcripts. Abundant IGF-Ir mRNA was found only in GC, IGF-IIr mRNA was found in both granulosa and thecal cells, and Ir mRNA was detected in all cell types, including granulosa, thecal, and stromal cells. Localization of the gene products revealed no IGF-I immunoreactivity; however, immunostaining for each of the other gene products was colocalized with its corresponding mRNA. The cellular distribution of mRNA and protein in PCOS follicles was indistinguishable from that observed in small antral follicles from normal ovaries. In dominant follicles, however, IGF-I mRNA was no longer detectable, but abundant IGF-II mRNA was expressed exclusively in GC. Although IGF-Ir mRNA was expressed in GC, IGF-IIr mRNA was found in both granulosa and thecal cells. In follicles taken from PCOS ovaries, no IGFBP-1 mRNA was detected, IGFBP-2 mRNA was abundant in both granulosa and thecal cells, moderate IGFBP-3 mRNA was found only in thecal cells, IGFBP-4 and -5 mRNAs were present in all cellular compartments, and IGFBP-6 mRNA was not detected. Localization of the gene products by immunostaining revealed that each protein colocalized with its corresponding mRNA. The cellular distribution of IGFBP mRNA and protein in PCOS follicles was also indistinguishable from that in small antral follicles of normal ovaries, but remarkable differences were found in dominant follicles, where abundant IGFBP-1 mRNA was seen exclusively in GC, IGFBP-2 mRNA in thecal cells, and IGFBP-3 mRNA in both granulosa and thecal cells. Moderate expression of the IGFBP-4 and **IGFBP-5** genes was seen in all cell types, including stromal cells, but no IGFBP-6 mRNA was detected. Again, each of the gene products colocalized with its corresponding mRNA. We conclude the following.(ABSTRACT TRUNCATED AT 400 WORDS)

L8 ANSWER 42 OF 42 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 95051819 MEDLINE
DOCUMENT NUMBER: 95051819 PubMed ID: 7516567
TITLE: Localization of messenger ribonucleic acid for insulin-like growth factor-binding proteins in human skin by in situ hybridization.
AUTHOR: Batch J A; Mercuri F A; Edmondson S R; Werther G A
CORPORATE SOURCE: Center for Hormone Research, University of Melbourne, Royal Children's Hospital, Parkville, Australia.

Journal code: HRB; 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950113
Last Updated on STN: 20000303
Entered Medline: 19941221

AB The role of the insulin-like growth factors (IGFs) in human skin physiology has been increasingly recognized, although relatively little is known about the cell types involved or the cellular mechanisms that mediate these responses. Epidermal keratinocytes and dermal fibroblasts both possess IGF-I receptors and are responsive to IGF-1. IGF-binding proteins (IGFBPs), known modulators of IGF action, may also be responsible for targeting IGF-I to its receptors and are produced by both cultured keratinocytes and fibroblasts. To demonstrate sites of production of IGFBPs in human skin, we have used in situ hybridization to localize messenger ribonucleic acid (mRNA) for the six IGFBPs. **Antisense** and sense RNA probes for the IGFBPs (IGFBP-1 to -6) were produced, and 5-microns sections of normal adult human male chest skin were probed. The control probe used was keratin-5, which is known to hybridize to the basal keratinocytes of the epidermis. mRNAs for human IGFBP-2, -3, -4, and -5 were identified, with mRNAs for IGFBP-2 and IGFBP-4 localized in sebaceous glands and eccrine sweat glands (epidermal origin). IGFBP-3 mRNA in the basal layer of the epidermis and mRNAs for IGFBP-4, and **IGFBP-5** found throughout the dermis. mRNAs for IGFBP-1 and -6 were not identified in human skin. These studies demonstrate specific localization of IGFBP mRNAs in adult human skin, suggesting that each IGFBP may play a specific role in targeting IGF-I to its receptor on responsive cells and, ultimately, in modulation of IGF-I action in skin.

=> d ibib kwic 10 12 14 19 18 29-29 31 32 33

L3 ANSWER 10 OF 42 USPATFULL
ACCESSION NUMBER: 2001:44198 USPATFULL
TITLE: Treatment of partial growth hormone insensitivity syndrome
INVENTOR(S): Attie, Kenneth M., San Francisco, CA, United States
Carlsson, Lena M. S., Gothenburg, Sweden
Gesundheit, Neil, Los Altos, CA, United States
Goddard, Audrey, San Francisco, CA, United States
PATENT ASSIGNEE(S): Genentech, Inc., South San Francisco, CA, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6174843	B1	20010127
APPLICATION INFO.:	US 1996-611212		19960318 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1995-411450, filed on 24 Mar 1995, now abandoned Continuation of Ser. No. US 1994-224982, filed on 7 Apr 1994, now patented, Pat. No. US 5646113		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jones, Dwayne C.
ASSISTANT EXAMINER: Delacroix-Muirheid, C.

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 44 [redacted]wing Figure(s); 38 Drawing Page(s)
LINE COUNT: 2469
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DETD . . . together with any one or more of its binding proteins, for example, those currently known, i.e., IGFBP-1, IGFBP-2, IGFBP-3, IGFBP-4, **IGFBP-5**, or IGFBP-6. The IGF-I may also be coupled to a receptor or antibody or antibody fragment for administration. The preferred. . .
DETD . . . exons 4-10 including the intron-exon boundaries were individually amplified by polymerase chain reaction (PCR) using primer pairs (of which the **antisense** was biotinilated) deduced from the published DNA sequence (3) (Sequences available on request). The PCR
products were submitted to direct. . .

L3 ANSWER 13 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2001:424132 BIOSIS
DOCUMENT NUMBER: PREV200100424132
TITLE: The IGF/IGFBP system in CNS malignancy.
AUTHOR(S): Zumkeller, W. (1); Westphal, M.
CORPORATE SOURCE: (1) Department of Pediatrics, Martin-Luther-University Halle-Wittenberg, University Hospital, Ernst-Grube-Str. 40, 06097, Halle/Saale: walter.zumkeller@medizin.uni-halle.de Germany
SOURCE: Molecular Pathology, (August, 2001) Vol. 54, No. 4, pp. 227-229. print.
ISSN: 1366-8714
DOCUMENT TYPE: Article
LANGUAGE: English.
SUMMARY LANGUAGE: English.
AB. . . are expressed in gliomas and, in particular, the type I IGF receptor
appears to be upregulated in malignant brain tissue. **Antisense** IGF-I receptor mRNA induces an antitumour response, resulting in complete brain tumour regression. Clinical trials for the treatment of brain tumours in humans based on a gene transfer protocol using IGF-I receptor **antisense** are under way. All six IGFBPs are expressed to a variable extent in brain tumours. High concentrations of IGFBP-2 are. . .
IT . . .
disease, nervous system disease; medulloblastoma: neoplastic disease, nervous system disease; meningioma: neoplastic disease, nervous system disease
IT Chemicals & Biochemicals
antisense insulin-like growth factor-I receptor messenger RNA; insulin-like growth factor binding protein-1; insulin-like growth factor binding protein-2; insulin-like growth factor binding protein-3;
insulin-like growth factor binding protein-4; **insulin-like growth factor binding protein 5**; insulin-like growth factor binding protein 6; insulin-like growth factor-I; insulin-like growth factor II;
type I insulin like growth factor receptor; type II insulin like. . .

L3 ANSWER 14 OF 42 USPATFULL
ACCESSION NUMBER: 2000:18550 USPATFULL
TITLE: Insulin like growth factor binding protein (IGFBP-6)
INVENTOR(S): Pfefer, Michael G., Clayton, CA, United States
Masiarz, Frank R., San Francisco, CA, United States
Zapf, Jurgen Johann Leopold, Zurich, Switzerland

corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6025468		20000215
APPLICATION INFO.:	US 1997-917204		19970825 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1990-576648, filed on 31 Aug 1990, now abandoned which is a division of Ser. No. US 1990-574613, filed on 28 Aug 1990, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Carlson, Karen Cochrane		
LEGAL REPRESENTATIVE:	Burns & Associates, Guth, Joseph H., Blackburn, Robert P.		
NUMBER OF CLAIMS:	4		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 6 Drawing Page(s)		
LINE COUNT:	1739		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DFWD . . . human IGFBP-4, to the known sequences of the three human binding proteins discussed above and another new human binding protein, **IGFBP-5**. Areas of homology can be seen in these sequences. These areas of homology are of particular interest as they indicated. . .

DETD . . . for IGFBP-6 were: (1) a "sense" primer consisting of a mixture of 64 27-mers [5' AGATCTGAATTCGCA(A/G)GGXGTXCA(A/G)GC 3'] and (2) an "**antisense**" primer consisting of a mixture of 64 28-mers [5' AGATCTGAATTCG(A/G)TC(C/T)TC(C/T)TC(C/T)TCXAC 3'] where X denotes all four deoxynucleotides. Eco RI sites. . .

L3 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1999:421772 CAPLUS
DOCUMENT NUMBER:	131:88554
TITLE:	Insulin-like growth factor binding protein fragments and their use in diagnosis and therapy
INVENTOR(S):	Forssmann, Wolf-Georg; Standker, Ludger; Obendorf, Maik; Kling, Lothar; Opitz, Hans-Georg; Mostafavi, Hossein
PATENT ASSIGNEE(S):	Germany
SOURCE:	PCT Int. Appl., 62 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9932620	A1	19990701	WO 1998-EP8405	19981222
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19757250	A1	1999[illegible]	DE 1997-19757250	19971222
CA 2315979	AA	1999[illegible]	CA 1998-2315979	19981222
EP 1044276	A1	2000[illegible]	EP 1998-965965	19981222
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE, IE				
JP 2002508931	T2	20020326	JP 2000-525539	19981222
PRIORITY APPLN. INFO.:			DE 1997-19757250 A	19971222
			WO 1998-EP8405 W	19981222

OTHER SOURCE(S): MARPAT 131:88554

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to IGFBP peptide-e[redacted]ding nucleic acid; insulin-lik[redacted]growth factor
binding protein fragments and their use in diagnosis [redacted]d therapy)
IT 220766-05-2P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological
process); BSU (Biological study, unclassified); PUR (Purification or
recovery); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); PROC (Process); USES (Uses)
(**IGFBP-5** fragment; insulin-like growth factor
binding protein fragments and their use in diagnosis and therapy)

L3 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:738627 CAPLUS
DOCUMENT NUMBER: 131:341964
TITLE: Compositions and methods for extending the action of clostridial neurotoxin and modulating neurite outgrowth in damaged neural endplates
INVENTOR(S): Dolly, J. Oliver; Aoki, Rei Roger; De Paiva, Anton
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955359	A1	19991104	WO 1999-US8303	19990415
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937484	A1	19991116	AU 1999-37484	19990415
EP 1073455	A1	20010207	EP 1999-919857	19990415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002512977	T2	20020518	JP 2000-545597	19990415
PRIORITY APPLN. INFO.:			US 1998-83472P P	19980429
			WO 1999-US8303 W	19990415

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT **Ribozymes**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(compns. and methods for extending the action of clostridial neurotoxin
and modulating neurite outgrowth in damaged neural endplates)
IT 155644-55-2, Glycoprotein IGF-BP 4 (human clone HBP4-509 precursor protein
moiety reduced) 136758-17-8, **Insulin-like growth factor-binding protein 5** (human
RL: BAC (Biological activity or effector, except adverse); BSU

unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(amino acid sequence; compns. and methods for extending the action of clostridial neurotoxin and modulating neurite outgrowth in damaged neural endplates)

L3 ANSWER 23 OF 42 USPATFULL
ACCESSION NUMBER: 1998:161109 USPATFULL
TITLE: TNF receptor death ligand proteins and inhibitors of ligand binding
INVENTOR(S): Lin, Li-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
Scheivella, Andrea R., Winchester, MA, United States
Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5852179		19981222
APPLICATION INFO.:	US 1995-533961		19950926 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-494440, filed on 19 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327914, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Walsh, Stephen		
ASSISTANT EXAMINER:	Kaufman, Claire M.		
LEGAL REPRESENTATIVE:	Sprunger, Suzanne A., Brown, Scott A., DesRosier, Thomas J.		
NUMBER OF CLAIMS:	7		
EXEMPLARY CLAIM:	7		
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)		
LINE COUNT:	1855		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and a protein selected from the group consisting of **insulin-like growth factor binding protein-5** (" **IGFBP-5** "), and fragments thereof having TNF-R1-DD ligand protein activity. Such proteins may also be administered for inhibiting TNF-R death domain. . .

DRWD FIG. 7 is an autoradiograph which demonstrates that an **antisense** oligonucleotide derived from the sequence of clone 3TW inhibits TNF-induced cPLA.sub.2 phosphorylation.

DETD The protein encoded by clone 20DD is identical to amino acids 87 to 272 of **insulin-like growth factor binding protein-5** ("**IGFBP-5**"), a sequence for which was disclosed in J. Biol. Chem. 266:10646-10653 (1991) by Shimasaki et al., which is incorporated herein by reference. The polynucleotide and amino acid sequences of **IGFBP-5** are set forth in SEQ ID NO:7 and SEQ ID NO:8, respectively. Based upon the sequence identity between clone 3 TW and **IGFBP-5**, **IGFBP 5** and certain fragments thereof will exhibit TNF-R1 DD ligand binding activity (as defined herein).

DETD Due to the similarity of their sequences to the insulin growth factor binding protein ("**IGFBP-5**") and fragments thereof which bind to the TNF-R death domain are proteins having TNF-R1-DD ligand protein activity as defined herein.. . .

DETD . . . homologies compared to Genbank and other databases.

Shimasaki et al., J. Biol. Chem. 266:10646-10653 (1991)) were isolated. The clones "22D," "3[redacted] and "20DD" were chosen for. [redacted].

DETD . . . TNF signaling can be established by lowering [redacted] eliminating the expression of the ligands. These experiments can be performed using **antisense** expression or transgenic mice.

DETD An **antisense** oligonucleotide was derived from the sequence of clone 3TW. The **antisense** oligonucleotide was assayed to determine its ability to inhibit TNF-induced pPLA.sub.2 phosphorylation.

FIG. 7 depicts the results of that experiment.. . . the anitsense oligonucleotide (3TWAS) was compared with the full-length clone (3TWFL), Flag-3TW full length (3TWFLflag) and pED-flag vector (pEDflag). The **antisense** oligonucleotide inhibited phosphorylation..

L6 ANSWER 24 OF 42 USPATFULL

ACCESSION NUMBER:	1998:157119 USPATFULL
TITLE:	TNF receptor death domain ligand proteins and method to identify inhibitors of ligand binding
INVENTOR(S):	Lin, Lih-Ling, Concord, MA, United States Chen, Jennifer, Chestnut Hill, MA, United States Schievella, Andrea R., Winchester, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5849501		19981215
APPLICATION INFO.:	US 1995-494440		19950614 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Walsh, Stephen
ASSISTANT EXAMINER:	Kaufman, Claire M.
LEGAL REPRESENTATIVE:	Brown, Scott A., Sprunger, Suzanne A., DesRosier, Thomas J.
NUMBER OF CLAIMS:	6
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	6 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT:	1627

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and a protein selected from the group consisting of **insulin like growth factor binding protein-5** ("**IGFBP-5**"), and fragments thereof having TNF-R1-DD ligand protein activity. Such proteins may also be administered for inhibiting TNF-R death domain binding.

DETD The protein encoded by clone 20DD is identical to amino acids 87 to 272 of **insulin like growth factor binding protein-5** ("**IGFBP-5**", a sequence for which was disclosed in . . . Biol. Chem. 266:10646-10653 (1991) by Shimasaki et al., which is incorporated herein by reference. The polynucleotide and amino acid sequences of **IGFBP-5** are set forth in SEQ ID NO:7 and SEQ ID NO:8, respectively. Based upon the sequence identity between clone 20DD and **IGFBP-5**, **IGFBP-5** and certain fragments thereof will exhibit TNF-R1-DD ligand binding activity (as defined herein).

DETD Due to the similarity of their sequences to the insulin growth factor

ligand protein activity as defined herein.. . .
DETD . . . homologies compared to Genbank and other databases.
Additionally, four other clones ("20DD") with identical sequence to a
portion of human **insulin-like growth**
factor binding protein-5 (Shunichi
Shimasaki et al., J. Biol. Chem. 266:10646-10653 (1991)) were isolated.
The clones "2DD," "3DD" and "21DD" were chosen for. . .
DETD . . . TNF signaling can be established by lowering or eliminating
the
expression of the ligands. These experiments can be performed using
antisense expression or transgenic mice.

L3 ANSWER 2 OF 42 USPATFULL
ACCESSION NUMBER: 1998:154396 USPATFULL
TITLE: TNF receptor death domain ligand proteins
INVENTOR(S): Lin, Lin-Ling, Concord, MA, United States
Chen, Jennifer, Chestnut Hill, MA, United States
PATENT ASSIGNEE(S): Genetics Institute, Inc., Cambridge, MA, United States
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5847099		19981208
APPLICATION INFO.:	US 1996-649341		19960517 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Walsh, Stephen
ASSISTANT EXAMINER: Kaufman, Claire M.
LEGAL REPRESENTATIVE: Brown, Scott A., DesRosier, Thomas J.
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 1242
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM . . . therapeutically effective amount of a composition comprising a
pharmaceutically acceptable carrier and a protein selected from the
group consisting of **insulin-like growth**
factor binding protein-5 ("
IGFBP-5"), and fragments thereof having TNF-R1-DD
ligand protein activity. Such proteins may also be administered for
inhibiting TNF-R death domain binding.
DETD The protein encoded by clone 21DD is identical to amino acids 37 to 272
of **insulin-like growth factor**
binding protein-5 ("**IGFBP-**
5"), a sequence for which was disclosed in J. Biol. Chem.
266:10646-10653 (1991) by Shimasaki et al., which is incorporated
herein
by reference. The polynucleotide and amino acid sequences of
IGFBP 5 are set forth in SEQ ID NO:7 and SEQ ID NO:8,
respectively. Based upon the sequence identity between clone 20DD and
IGFBP 5, **IGFBP 5** and certain
fragments thereof will exhibit TNF-R1-DD ligand binding activity (as
defined herein).
DETD . . . Due to the similarity of their sequences to the insulin growth factor
binding protein 5 ("**IGFBP 5**") and fragments thereof
which bind to the TNF-R death domain are proteins having TNF-R1-DD
ligand protein activity as defined herein.. . .
DETD . . . homologies compared to Genbank and other databases.
Additionally, four other clones ("20DD") with identical sequence to a
portion of human **insulin-like growth**
factor binding protein-5 (Shunichi
Shimasaki et al., J. Biol. Chem. 266:10646-10653 (1991)) were isolated.

expression of the ligands. These experiments can be performed using **antisense** expression or transgenic mice.

L3 ANSWER 26 OF 42 USPATFULL

ACCESSION NUMBER:	1998:150692 USPATFULL
TITLE:	TNF receptor death domain ligand proteins and inhibitors of ligand binding
INVENTOR(S):	Lin, Li-Ling, Concord, MA, United States Chen, Jennifer, Chestnut Hill, MA, United States Somerville, Andrea R., Winchester, MA, United States Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5843679		19981201
APPLICATION INFO.:	US 1996-602123		19960215 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1995-553901, filed on 26 Sep 1995 which is a continuation-in-part of Ser. No. US 1995-496440, filed on 29 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Lim, John		
LEGAL REPRESENTATIVE:	Sprunger, Suzanne A., Brown, Scott A.		
NUMBER OF CLAIMS:	16		
EXEMPLARY CLAIM:	6		
NUMBER OF DRAWINGS:	8 Drawing Figure(s); 8 Drawing Page(s)		
LINE COUNT:	2125		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and a protein selected from the group consisting of **insulin-like growth factor binding protein-5** (" **IGFBP-5**"), and fragments thereof having TNF-R1-DD ligand protein activity. Such proteins may also be administered for inhibiting TNF-R death domain binding.

DRWD FIG. 7 is an autoradiograph which demonstrates that an **antisense** oligonucleotide derived from the sequence of clone 3TW inhibits TNF-induced cPLA.sub.. phosphorylation.

DETD The protein encoded by clone 20DD is identical to amino acids 87 to 272 of **insulin-like growth factor binding protein-5** ("**IGFBP-5**"), a sequence for which was disclosed in J. Biol. Chem. 266:10646-10653 (1991) by Shimasaki et al., which is incorporated herein by reference. The polynucleotide and amino acid sequences of **IGFBP 5** are set forth in SEQ ID NO:7 and SEQ ID NO:8, respectively. Based upon the sequence identity between clone 20DD and **IGFBP 5**, **IGFBP-5** and certain fragments thereof will exhibit TNF-R, DD ligand binding activity (as defined herein).

DETD Due to the similarity of their sequences to the insulin growth factor binding protein ("**IGFBP 5**") and fragments thereof which bind to the TNF R death domain are proteins having TNF-R1 DD ligand protein activity as defined herein. . . .

DETD . . . homologies compared to Genbank and other databases. Additionally, four other clones ("20DD", with identical sequence to a portion of human **insulin-like growth factor binding protein-5** Shunichi Shimasaki et al., J. biol. Chem. 266:10646-10653 (1991)) were isolated. The clones "20D," "3TW" and "20DD" were chosen for . . .

expression of the ligands. These experiments can be performed using **antisense** expression in transgenic mice.

DETD An **antisense** oligonucleotide was derived from the sequence of clone pTW. The **antisense** oligonucleotide was assayed to determine its ability to inhibit TNF-induced cPLA.sub.2 phosphorylation.

FIG. 7 depicts the results of that experiment. . . . the antisense oligonucleotide (pTWAS) was compared with the full-length clone (pTWFL), Flag-pTW full length (pTWFLflag) and pED-flag vector (pEDflag). The **antisense** oligonucleotide inhibited phosphorylation.

L3 ANSWER 2? OF 42 USPATFULL

ACCESSION NUMBER:	1999:41043 USPATFULL
TITLE:	Methods and reagents for the identification and regulation of senescence-related genes
INVENTOR(S):	Linskens, Maarten H. K., Palo Alto, CA, United States Hirsch, Kenneth S., Palo Alto, CA, United States Villeponteau, Bryant, San Carlos, CA, United States Feng, Junli, San Carlos, CA, United States Funk, Walter, Union City, CA, United States West, Michael David, Belmont, CA, United States
PATENT ASSIGNEE(S):	Geron Corporation, Menlo Park, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5744300		19980428
APPLICATION INFO.:	US 1994-338420		19941031 (8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1994-235180, filed on 29 Apr 1994, now patented, Pat. No. US 5580726 And Ser. No. US 1993-38766, filed on 24 Mar 1993, now patented, Pat. No. US 5489509		

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Myers, Carla J.
LEGAL REPRESENTATIVE:	Kaster, KevinLyon & Lyon LLP
NUMBER OF CLAIMS:	19
EXEMPLARY CLAIM:	1
LINE COUNT:	2409

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . no. 01M5); MITHS (encodes mitochondrial RNA, band no. 02A2); HUMTFPA (encodes human tissue factor, band no. 06E1); HUMIGFBP5 (encodes human **insulin-like growth factor binding protein 5**, band no. 07J1; band no. 11H1 corresponds to GenBank locus HUMIGFBP5X); HUMSGP3 (encodes human secretory granule core proteoglycan, also known. . . .

SUMM . . . techniques of molecular biology, not only to express the mRNA or protein encoded by the gene but also to express **antisense** oligonucleotides or **ribozymes** that can be used to prevent deleterious expression of senescence-related genes. Those of skill in the art recognize that a. . . .

L3 ANSWER 2? OF 42 USPATFULL

ACCESSION NUMBER:	1998:6502 USPATFULL
TITLE:	MADD, a TNF receptor death domain ligand protein
INVENTOR(S):	Lin, Lih-Ling, Concord, MA, United States Chen, Jennifer, Chestnut Hill, MA, United States Schievella, Andrea R., Winchester, MA, United States Graham, James, Somerville, MA, United States
PATENT ASSIGNEE(S):	Genetics Institute, Inc., Cambridge, MA, United States (U.S. corporation)

PATENT INFORMATION: US 5712391 19980127
APPLICATION INFO.: US [redacted]6-699551 19960815 (8[redacted]
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1996-602228, filed on 15 Feb 1996 which is a continuation-in-part of Ser. No. US 1995-533911, filed on 26 Sep 1995 which is a continuation-in-part of Ser. No. US 1995-494440, filed on 14 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-327514, filed on 19 Oct 1994, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Walsh, Stephen
ASSISTANT EXAMINER: Ranjan, Mukul
LEGAL REPRESENTATIVE: Brown, Scott A., Sprunger, Suzanne A., DesRosier, Thomas J.
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)
LINE COUNT: 1819
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . therapeutically effective amount of a composition comprising a pharmaceutically acceptable carrier and a protein selected from the group consisting of **insulin-like growth factor binding protein-5** ("**IGFBP-5**"), and fragments thereof having TNF-R1-DD ligand protein activity. Such proteins may also be administered for inhibiting TNF-R death domain binding.

DRWD FIG. 7 is an autoradiograph which demonstrates that an **antisense** oligonucleotide derived from the sequence of clone 3TW inhibits TNF-induced cPLA.sub.2 phosphorylation.

DETD The protein encoded by clone 20DD is identical to amino acids 87 to 272 of **insulin-like growth factor binding protein-5** ("**IGFBP-5**"), a sequence for which was disclosed in J. Biol. Chem. 266:10646-10653 (1991) by Shimasaki et al., which is incorporated herein by reference. The polynucleotide and amino acid sequences of **IGFBP-5** are set forth in SEQ ID NO:7 and SEQ ID NO:8, respectively. Based upon the sequence identity between clone 20DD and **IGFBP-5**, **IGFBP-5** and certain fragments thereof will exhibit TNF-R1 -DD ligand binding activity (as defined herein).

DETD Due to the similarity of their sequences to the insulin growth factor binding protein ("**IGFBP-5**") and fragments thereof which bind to the TNF-R death domain are proteins having TNF-R1-DD ligand protein activity as defined herein.. . .

DETD . . . homologies compared to Genbank and other databases. Additionally, four other clones ("20DD" with identical sequence to a portion of human **insulin-like growth factor binding protein-5** (Shunichi Shimasaki et al., J. Biol. Chem. 266:10646-10653 (1991)) were isolated. The clones "2DD," "3TP" and "20DD" were chosen for. . .

DETD . . . TNF signaling can be established by lowering or eliminating the expression of the ligands. These experiments can be performed using **antisense** expression or transgenic mice.

DETD An **antisense** oligonucleotide was derived from the sequence of clone 3TW. The **antisense** oligonucleotide was assayed to determine its ability to inhibit TNF-induced cPLA.sub.2 phosphorylation.

PIG. 7 depicts the results of that experiment.. . . the antisense oligonucleotide ("3TWAS") was compared with the full-length clone ("3TWFL"), Flag-TW full length ("3TWFLflag") and pFLAG flag vector ("pFLflag"). The

L? ANSWER 31 OF 42 MEDLINE
ACCESSION NUMBER: 97207956 MEDLINE
DOCUMENT NUMBER: 97207956 PubMed ID: 9139435
TITLE: Insulin-like growth factor binding protein gene expression in the pregnant rat uterus and placenta.
AUTHOR: Serra J A; Pinter J E
CORPORATE SOURCE: Department of Anatomy and Cell Biology, Columbia University
College of Physicians and Surgeons, New York, New York 10032, USA.
CONTRACT NUMBER: NS21970 (NINDS)
SOURCE: DEVELOPMENTAL BIOLOGY, (1997 Apr 15) 184 (2) 278-95.
Journal code: E7T; 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19970612
Entered Medline: 19970602
AB . . . example, IGFBP-4 is expressed in the inner circular layer shortly
after implantation, and expression increases through late gestation. In contrast, **IGFBP-5** hybridization occurs over both myometrial layers before implantation, but decreases in intensity and spatial distribution as pregnancy proceeds. Finally, and. . .
CT . . .
Hybridization
Microscopy, Video
Myometrium: ME, metabolism
Nucleic Acid Hybridization
Placenta: CY, cytology
*Placenta: ME, metabolism
Pregnancy
Preimplantation Phase
Protein Binding
RNA, Antisense: ME, metabolism
RNA, Messenger: GE, genetics
RNA, Messenger: ME, metabolism
Rats
Rats, Sprague-Dawley
Receptors, Somatomedin: BI, biosynthesis
*Receptors, . . .
CR 0 (RNA, **Antisense**); 0 (RNA, Messenger ; 0 (Receptors, Somatomedin)

L? ANSWER 32 OF 42 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:372393 BIOSIS
DOCUMENT NUMBER: PREV199799672186
TITLE: In vitro and in vivo studies on the role of insulin-like growth factor binding protein-3, -4 and -5 on bone formation.
AUTHOR(S): Kanzaki, S. (1); Mohan, S.; Ono, T. (1); Matsuoka, Y. (1); Moriwake, T. (1); Tanaka, H. (1); Seino, Y. (1)
CORPORATE SOURCE: (1) Dep. Pediatrics, Okayama Univ. Med. Sch., Okayama 7 Japan
SOURCE: Hormone Research (Basel), (1997) Vol. 48, No. SUPPL. 2, pp.
16.
Meeting Info.: 5th Joint Meeting of the European Society for Paediatric Endocrinology and the Lawson Wilkins Society
for Pediatric Endocrinology, in Collaboration with the

for Pediatric Endocrinology and the Latin American Society for Pae[redacted]tric Endocrinology Stockholm, [redacted]den June 22-26, 1997
ISSN: 0301-0163.
DOCUMENT TYPE: Conference; Abstract
LANGUAGE: English
IT . . .
LYMPHATICS; BONE; BONE DISEASE; BONE MINERAL DENSITY; ENDOCRINE SYSTEM;
FORMATION; INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3; INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3 **ANTISENSE** OLIGONUCLEOTIDE; INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-4; INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-4 **ANTISENSE** OLIGONUCLEOTIDE;
INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-5; OSTEOPENIA; SENSORY SYSTEM; SKELETAL SYSTEM

L3 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:211409 CAPLUS
DOCUMENT NUMBER: 124:270541
TITLE: Use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment of proliferative and/or inflammatory skin disorders
INVENTOR(S): Werther, George Arthur; Wraight, Christopher John
PATENT ASSIGNEE(S): Rcya. Children's Hospital Research Foundation, Australia
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9601636	A1	19960125	WO 1995-AU410	19950706
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2194366	AA	19960125	CA 1995-2194366	19950706
AU 9528753	A1	19960209	AU 1995-28753	19950706
AU 694274	B2	19980604		
EP 770210	A1	19970604	EP 1995-924110	19950706
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 11508296	T2	19980818	JP 1995-504013	19950706
US 5919041	A	19990727	US 1996-666392	19960820
US 6, 4741	B1	[illegible]	US 1999-[illegible]	19991125

PRIORITY APPLN. INFO.: AU 1994-6725 A 19940706
WO 1995-AU410 W 19950706
US 1996-666392 A1 19960820

TI Use [illegible] **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment of proliferative and/or inflammatory skin disorders
AB The present invention relates generally to a method for the prophylaxis and/or treatment of skin disorders, and in particular proliferative and/or inflammatory skin disorders, and to nucleic acids or nucleic acid analogs useful for same. The present invention is particularly directed to mole

stimulation of this layer of cells. The present invention contemplates, in a most preferred embodiment, a method for the prophylaxis and/or treatment of psoriasis. Phosphorothioate-linked oligonucleotide (18- and 24-mers) **antisense** to human insulin-like growth factor binding protein 3-encoding nucleic acid inhibited IGFBP-3 synthesis by HaCaT cells
(human differentiated keratinocyte cell line).

ST skin disorder proliferative inflammatory treatment; **antisense** oligonucleotide inhibition growth factor proliferation; insulin like growth factor **antisense** oligonucleotide; psoriasis treatment **antisense** oligonucleotide growth factor

IT Animal growth regulator receptors
RL: MSC (Miscellaneous)
(antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Skin, disease
(proliferative or inflammatory; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Keloid
Keratosis
Psoriasis
Seborrhea
Skin, neoplasm
Wart
(use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT **Ribozymes**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Proteins, specific or class
RL: MSC (Miscellaneous)
(IGF-BP-2 (insulin-like growth factor-binding protein 2), antagonism of
cell proliferation related to; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Glycoproteins, specific or class
RL: MSC (Miscellaneous)
(IGF-BP-3 (insulin-like growth factor-binding protein 3), antagonism of
cell proliferation related to; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Glycoproteins, specific or class
RL: MSC (Miscellaneous)
(IGF-BP-4 (insulin-like growth factor-binding protein 4), antagonism of
cell proliferation related to; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders

IT Proteins, specific or class
RL: MSC (Miscellaneous)
(IGF-BP-5 (**insulin-like growth factor binding protein 5**), antagonism of cell proliferation related to; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT Glycoproteins, specific or class
RL: MSC (Miscellaneous)
(IGF-BP-6 (insulin-like growth factor-binding protein 6), antagonism of

treatment skin disorders)
IT Receptors
RL: MSC (Miscellaneous)
(animal growth regulator, antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)
IT Connective tissue
(disease, scleroderma, use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin
disorders)
IT Skin, disease
(ichthyosis, use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin
disorders)
IT Receptors
RL: MSC (Miscellaneous)
(insulin-like growth factor I, antagonism of cell proliferation induced
by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)
IT Proteins, specific or class
RL: MSC (Miscellaneous)
(insulin-like growth factor-binding, antagonism of cell proliferation related to; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin
disorders)
IT Lymphokines and Cytokines
RL: MSC (Miscellaneous)
(interleukin 1, antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)
IT Lymphokines and Cytokines
RL: MSC (Miscellaneous)
(interleukin 4, antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)
IT Lymphokines and Cytokines
RL: MSC (Miscellaneous)
(interleukin 6, antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)
IT Lymphokines and Cytokines
RL: MSC (Miscellaneous)
(interleukin 8, antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)
IT Nucleotides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligo-, **antisense**; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)
IT Skin, disease
(pityriasis, use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin
disorders)
IT Lymphokines and Cytokines
RL: MSC (Miscellaneous)
(tumor necrosis factor-.alpha., antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor mediated cell proliferation for treatment skin
disorders)

(.alpha.-transforming growth factors, antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT 67763-96-6, Insulin-like growth factor I 106196-93-9, Basic fibroblast growth factor 148848-15-6, Fibroblast growth factor 7
RL: MSC (Miscellaneous)
(antagonism of cell proliferation induced by; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT 140029-74-9, GenBank M31159 140068-68-4, GenBank X04434 140079-08-9, GenBank X16302
RL: MSC (Miscellaneous)
(**antisense** oligonucleotides in relation to; use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)

IT 175338-58-6 175338-59-7 175338-60-0 175338-61-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **antisense** nucleic acids/analogs inhibiting growth factor-mediated cell proliferation for treatment skin disorders)